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dis his

     (FILE 'HOME' ENTERED AT 15:37:34 ON 20 FEB 2002)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 15:46:02 ON 20 FEB 2002
L1           851 S NOTCH (2N) LIGAND?
L2           337 S L1 AND PD<19990405
L3             0 S L2 (10N) ADMINIST?
L4             0 S L2 (P) ADMINIST?
L5         29095 S NOTCH
L6          2162 S L5 AND (SERRATE OR DELTA)
L7           763 S L6 AND RECEPTOR?
L8             0 S L7 AND ADMINISTR?
L9             0 S L7 AND ADMINIST?
L10            0 S L1 AND ADMINIST?
L11          268 S L5 AND ADMINIST?
L12          148 S L11 AND PD<19990504
L13          111 DUP REM L12 (37 DUPLICATES REMOVED)
L14            4 S L13 AND (DELTA OR SERRATE)

=> s l13 not (EEG or EKG or ventricul?)
L15           90 L13 NOT (EEG OR EKG OR VENTRICUL?)

=> dis l15 1-90 ibib abs kwic
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Connecting via Winsock to STN

Trying 3106016892...Open

Welcome to STN International!  Enter x:x
LOGINID:ssspta1644axd
PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Sep 17   IMSworld Pharmaceutical Company Directory name change
                   to PHARMASEARCH
 NEWS  3  Oct 09   Korean abstracts now included in Derwent World Patents
                   Index
 NEWS  4  Oct 09   Number of Derwent World Patents Index updates increased
 NEWS  5  Oct 15   Calculated properties now in the REGISTRY/ZREGISTRY File
 NEWS  6  Oct 22   Over 1 million reactions added to CASREACT
 NEWS  7  Oct 22   DGENE GETSIM has been improved
 NEWS  8  Oct 29   AAASD no longer available
 NEWS  9  Nov 19   New Search Capabilities  USPATFULL and USPAT2
 NEWS 10  Nov 19   TOXCENTER(SM) - new toxicology file now available on STN
 NEWS 11  Nov 29   COPPERLIT now available on STN
 NEWS 12  Nov 29   DWPI revisions to NTIS and US Provisional Numbers
 NEWS 13  Nov 30   Files VETU and VETB to have open access
 NEWS 14  Dec 10   WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
 NEWS 15  Dec 10   DGENE BLAST Homology Search
 NEWS 16  Dec 17   WELDASEARCH now available on STN
 NEWS 17  Dec 17   STANDARDS now available on STN
 NEWS 18  Dec 17   New fields for DPCI
 NEWS 19  Dec 19   CAS Roles modified
 NEWS 20  Dec 19   1907-1946 data and page images added to CA and CAplus
 NEWS 21  Jan 25   BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS 22  Jan 25   Searching with the P indicator for Preparations
 NEWS 23  Jan 29   FSTA has been reloaded and moves to weekly updates
 NEWS 24  Feb 01   DKILIT now produced by FIZ Karlsruhe and has a new update
                   frequency
 NEWS 25  Feb 19   Access via Tymnet and SprintNet Eliminated Effective 3/31/02

 NEWS EXPRESS   February 1 CURRENT WINDOWS VERSION IS V6.0d,
                CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
                AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS     STN Operating Hours Plus Help Desk Availability
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FILE 'HOME' ENTERED AT 15:37:34 ON 20 FEB 2002

=> file medline caplus embase biosis
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     2.10       2.10

FILE 'MEDLINE' ENTERED AT 15:46:02 ON 20 FEB 2002

FILE 'CAPLUS' ENTERED AT 15:46:02 ON 20 FEB 2002
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FILE 'BIOSIS' ENTERED AT 15:46:02 ON 20 FEB 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

=> s notch (2N) ligand?
L1          851 NOTCH (2N) LIGAND?

=> s l1 and PD<199990405
'199990405' NOT A VALID FIELD CODE
DATE SPECIFICATION IS NOT VALID
DATE SPECIFICATION IS NOT VALID
DATE SPECIFICATION IS NOT VALID
Date specifications may use ranges and numeric operators.  The date
itself can be in any of the following general formats:

   STN Format:     YYYYMMDD

   Slash Format:   MM/DD/YYYY or MM/YYYY

   Dot Format:     DD.MM.YYYY or MM.YYYY

   Text Format:    February 10, 1987       Feb 1989
                   Feb. 10, 1987           1990
                   Feb. 10, 2000           1998 - 2001
                   Feb 10, 1987            July 1997 - May 2002
                   10 February 1987        March 5 - 8, 1990
                   10 Feb 2007             April - June, 1999

   Any year entered with only two digits will be interpreted as being
   in the range 1900-1999.  Thus, Mar 12 01 will be searched as
   19010312.
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```
=> s l1 and PD<19990405
'19990405' NOT A VALID FIELD CODE
   3 FILES SEARCHED...
L2          337 L1 AND PD<19990405

=> s l2 (10N) administ?
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L6  (10A) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L7  (10A) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L8  (10A) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L9  (10A) ADMINIST?'
L3            0 L2 (10N) ADMINIST?

=> s l2 (P) administ?
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L6  (P) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L7  (P) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L8  (P) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L9  (P) ADMINIST?'
L4            0 L2 (P) ADMINIST?

=> s notch
L5        29095 NOTCH

=> s l5 and (serrate or delta)
L6         2162 L5 AND (SERRATE OR DELTA)

=> s l6 and receptor?
L7          763 L6 AND RECEPTOR?

=> s l7 and administr?
L8            0 L7 AND ADMINISTR?

=> s l7 and administ?
L9            0 L7 AND ADMINIST?

=> s l1 and administ?
L10           0 L1 AND ADMINIST?

=> s l5 and administ?
L11         268 L5 AND ADMINIST?

=> s l11 and PD<19990504
'19990504' NOT A VALID FIELD CODE
   3 FILES SEARCHED...
L12         148 L11 AND PD<19990504

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13          111 DUP REM L12 (37 DUPLICATES REMOVED)

=> s l13 and (delta or serrate
UNMATCHED LEFT PARENTHESIS 'AND (DELTA'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s l13 and (delta or serrate)
L14           4 L13 AND (DELTA OR SERRATE)

=> dis l14 1-4 ibib abs kwic

L14  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         1994:426887  CAPLUS
DOCUMENT NUMBER:          121:26887
TITLE:                    Therapeutic and diagnostic methods and compositions
                          based on Notch proteins and nucleic acids
INVENTOR(S):              Artavanis-Tsakonas, Spyridon; Fehon, Richard Grant;
                          Zagouras, Panayiotis; Blaumueller, Christine Marie
PATENT ASSIGNEE(S):       Yale University, USA
SOURCE:                   PCT Int. Appl., 232 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 9407474         A1   19940414       WO 1993-US9338   19930930 <--
         W:  AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN,
             MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ, VN
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
             BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
     US 5786158         A    19980728       US 1993-83590    19930625 <--
     EP 662827          A1   19950719       EP 1993-923752   19930930 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
     JP 08502170        T2   19960312       JP 1993-509326   19930930 <--
     AU 685067          B2   19980115       AU 1994-53503    19930930 <--
PRIORITY APPLN. INFO.:                    US 1992-955012   A2 19920930
                                          US 1993-83590    A2 19930625
                                          US 1992-879038   B2 19920430
                                          WO 1993-US9338   W  19930930
AB   Therapeutic and diagnostic methods and compns. based on Notch
     proteins and nucleic acids are provided.  The sequences of human
     Notch cDNA and the encoded human Notch protein are also
     disclosed.  The invention provides treatment of disorders of cell fate or
     differentiation by administration of a therapeutic compd. of the
     invention.  Such therapeutic compds. include Notch proteins and
     analogs and derivs. (including fragments) thereof, antibodies thereto,
     nucleic acids encoding the Notch proteins, analogs, or derivs.,
     Notch antisense nucleic acids, as well as toporythmic proteins and
     derivs. which bind to or otherwise interact with Notch proteins,
     their encoding nucleic acids or antibodies.  The therapeutic is
     administered to treat a cancerous condition, or to prevent
     progression from a pre-neoplastic or non-malignant state into a neoplastic
     or a malignant state.
TI   Therapeutic and diagnostic methods and compositions based on Notch
```

proteins and nucleic acids

PI WO 9407474 A1 **19940414**

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9407474	A1	19940414	WO 1993-US9338	19930930 <--
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5786158	A	19980728	US 1993-83590	19930625 <--
EP 662827	A1	19950719	EP 1993-923752	19930930 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08502170	T2	19960312	JP 1993-509326	19930930 <--
AU 685067	B2	19980115	AU 1994-53503	19930930 <--

AB Therapeutic and diagnostic methods and compns. based on **Notch** proteins and nucleic acids are provided. The sequences of human **Notch** cDNA and the encoded human **Notch** protein are also disclosed. The invention provides treatment of disorders of cell fate or differentiation by **administration** of a therapeutic compd. of the invention. Such therapeutic compds. include **Notch** proteins and analogs and derivs. (including fragments) thereof, antibodies thereto, nucleic acids encoding the **Notch** proteins, analogs, or derivs., **Notch** antisense nucleic acids, as well as toporythmic proteins and derivs. which bind to or otherwise interact with **Notch** proteins, their encoding nucleic acids or antibodies. The therapeutic is **administered** to treat a cancerous condition, or to prevent progression from a pre-neoplastic or non-malignant state into a neoplastic or a malignant state.

ST human **Notch** protein therapeutic; cDNA antibody human **Notch**

IT Alopecia
Cirrhosis
Keloid
Psoriasis
(**Notch** protein as diagnosistics and)

IT Gene, animal
RL: BIOL (Biological study)
(cDNA, for human **Notch** protein and Drosophila **Delta** protein)

IT Protein sequences
(of human **Notch** protein and Drosophila **Delta** protein)

IT Antibodies
RL: BIOL (Biological study)
(to human **Notch** protein, for diagnostics and therapeutics)

IT Gene, animal
RL: BIOL (Biological study)
(**Serrate**, protein of, **Notch** protein as therapeutics in relation to)

IT Uterus, neoplasm
(cervix, treatment and diagnosis of, **Notch** protein as diagnosistics and)

IT Neoplasm inhibitors
(colon, **Notch** protein as diagnosistics and)

IT Intestine, neoplasm
(colon, inhibitors, **Notch** protein as diagnosistics and)

IT Deoxyribonucleic acid sequences
(complementary, for human **Notch** protein and Drosophila **Delta** protein)

IT Deoxyribonucleic acids
RL: BIOL (Biological study)
(complementary, antisense, of human **Notch** gene, for diagnostics and therapeutics)

IT Proteins, specific or class
RL: BIOL (Biological study)
(gene **Delta**, **Notch** protein as therapeutics in relation to)

IT Lung, neoplasm
(inhibitors, **Notch** protein as diagnosistics and)

IT Neoplasm inhibitors
(lung, **Notch** protein as diagnosistics and)

IT Neoplasm inhibitors
(mammary gland, **Notch** protein as diagnosistics and)

IT Neoplasm inhibitors
(melanoma, **Notch** protein as diagnosistics and)

IT Antibodies
RL: BIOL (Biological study)
(monoclonal, to human **Notch** protein, for diagnostics and therapeutics)

IT Mammary gland
(neoplasm, inhibitors, **Notch** protein as diagnosistics and)

IT Testis, neoplasm
(seminoma, treatment and diagnosis of, **Notch** protein as diagnosistics and)

IT 146636-21-7, **Delta** protein (Drosophila)
RL: PRP (Properties)
(amino acid sequence of)

IT 146636-19-3, **Notch** protein fragment (Drosophila)
RL: BIOL (Biological study)
(human **Notch** protein homologous to, as therapeutics)

IT 148513-28-4, DNA (Drosophila **Delta** cDNA D11) 156067-52-6 156067-53-7 156067-54-8 156067-55-9
RL: PRP (Properties)
(nucleotide sequence of)

IT 146636-08-0, DNA (human clone hN2k **Notch** protein fragment encoding cDNA) 146636-13-7, DNA (human clone hN2k **Notch** protein fragment encoding cDNA) 156067-43-5 156067-44-6 156067-45-7
RL: PRP (Properties)
(nucleotide sequence of, therapeutics contg. protein encoded by)

L14 ANSWER 2 OF 4 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 77031163 EMBASE
DOCUMENT NUMBER: 1977031163
TITLE: [An unusual electroclinical event during one case of L Dopa treatment].
A PROPOS D'UN ASPECT ELECTROCLINIQUE PARTICULIER OBSERVE DANS LE COURS D'UN TRAITEMENT A LA L DOPA.
AUTHOR: Lavaivre M.; Sainty J.M.; Conte Devolx J.; et al.
CORPORATE SOURCE: Serv. EEG, Secteur Sud, CHU, Marseille, France
SOURCE: Revue d'E.E.G. et de Neuro-Physiologie Clinique, (1975) 5/4 (395-398).
CODEN: RENCBH
DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
030 Pharmacology
LANGUAGE: French

AB A woman of 62 had suffered from Parkinson's disease from the age of 40 and had been treated with L Dopa in a dosage of 4 g. daily. On 3 occasions during this treatment she had developed more or less severe cardiorespiratory distress. In the most alarming attack, with cyanosis, polypnoea, struggling for breath, and cardiovascular collapse, necessitating intubation with the **administration** of corticoids and tranquillizers, the EEG showed, besides a dysrhythmia some sinusoidal **delta** waves, with steep gradients and an amplitude up to 100-150 microvolts with **notches** on the crest. These abnormalities appear in bifrontal hypersynchronised bursts at 2-2.5 cycles per sec. The visual reaction of arrest is present for the alpha rhythm, to a degree which declines for the slow activities. After 24 hours, the EEG returns to normal while the calm patient once more shows a Parkinsonian tremor. The authors discuss the relationship between cardiorespiratory disorders and EEG anomalies as shown in their patient, with the signs of intolerance to L Dopa already described in the literature. (Isch - Strasbourg)

SO Revue d'E.E.G. et de Neuro-Physiologie Clinique, (1975) 5/4 (395-398).
CODEN: RENCBH

AB . . . cardiorespiratory distress. In the most alarming attack, with cyanosis, polypnoea, struggling for breath, and cardiovascular collapse, necessitating intubation with the **administration** of corticoids and tranquillizers, the EEG showed, besides a dysrhythmia some sinusoidal **delta** waves, with steep gradients and an amplitude up to 100-150 microvolts with **notches** on the crest. These abnormalities appear in bifrontal hypersynchronised bursts at 2-2.5 cycles per sec. The visual reaction of arrest. . .

CT Medical Descriptors:
*adverse drug reaction
*clinical study
*collapse
*electroencephalography
*hyaline membrane disease
*parkinson disease
*drug therapy
*respiratory failure
major clinical study
therapy
oral drug administration
*levodopa

L14 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1991:133230 BIOSIS
DOCUMENT NUMBER: BA91:69770
TITLE: THE WOLFF-PARKINSON-WHITE SYNDROME IN A HOLSTEIN-FRIESIAN COW.
AUTHOR(S): ENDO Y; TAJIMA M; KUROSAWA T; TAKAHASHI K; SONODA M
CORPORATE SOURCE: DEP. VETERINARY INTERNAL MED., RAKUNO GAKUEN UNIV., EBETSU 069, JPN.
SOURCE: JPN J VET SCI, (1990) 52 (6), 1155-1162.
CODEN: NJUZA9. ISSN: 0021-5295.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB A case of Wolff-Parkinson-White (WPW) syndrome in a Holstein-Friesian cow aged 10-year-old was examined in detail. In electrocardiogram (ECG), the P-wave was the same configuration in both the normal and abnormal ECG. The PR-interval shortened from 0.2 to 0.1 second and the duration of the QRS-complex prolonged from 0.1 to 0.12 second compared with normal ECG. The **delta** wave, characterized in WPW syndrome, could not be recognized. In echocardiogram, **notches** were recognized at the early stage of ventricular contraction in the interventricular septum. This cow was, therefore, diagnosed as type B WPW syndrome. The abnormal ECG disappeared by the **administration** of procainamide. It was strongly indicated that the ventricular contraction showing abnormal ECG was generated only by the stimulation through an accessory pathway in this cow.

SO JPN J VET SCI, (1990) 52 (6), 1155-1162.
CODEN: NJUZA9. ISSN: 0021-5295.

AB. . . to 0.1 second and the duration of the QRS-complex prolonged from 0.1 to 0.12 second compared with normal ECG. The **delta** wave, characterized in WPW syndrome, could not be recognized. In echocardiogram, **notches** were recognized at the early stage of ventricular contraction in the interventricular septum. This cow was, therefore, diagnosed as type B WPW syndrome. The abnormal ECG disappeared by the **administration** of procainamide. It was strongly indicated that the ventricular contraction showing abnormal ECG was generated only by the stimulation through. . .

L14 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1987:445325 BIOSIS
DOCUMENT NUMBER: BA84:101163
TITLE: A CLINICAL STUDY OF THE SECOND COMPONENT OF LEFT VENTRICULAR SYSTOLIC PRESSURE.
AUTHOR(S): TAKAZAWA K
CORPORATE SOURCE: DEP. INTERN. MED., TOKYO MED. COLL.
SOURCE: J TOKYO MED COLL, (1987) 45 (2), 256-270.
CODEN: TIDZAH. ISSN: 0040-8905.
FILE SEGMENT: BA; OLD
LANGUAGE: Japanese

AB Arterial and left ventricular systolic pressure are divided into two components by the anacrotic **notch**. The first component is mainly caused by the left ventricular ejection and the second component by the peripheral reflection wave. The increase in the second component of the left ventricular pressure comes after the peak of the left ventricular ejection and is probably a part of excessive left ventricular afterload. The purpose of this study was to compare the second component of the left ventricular pressure and investigate the changes after an intravenous injection of angiotensin and a sublingual **administration** of nitroglycerin. Forty-nine patients, 18 with myocardial infarction (MI group), 20 with angina pectoris (AP group) and 11 others (Ot group) were studied. The pressure in the left ventricle and at the base of the ascending aorta were measured by means of a micromanometer-tipped catheter (Miller-PC-484A) in the subjects' normal conditions and after an intravenous injection of 2.5 .mu.g angiotensin and a sublingual **administration** of 0.3 mg nitroglycerin. Aortic reflection wave ratio (AoRWR) and left ventricular reflection wave ratio (LVRWR) were expressed as follows: (AoRWR) = (late peak aortic systolic pressure-pressure at anacrotic **notch**)/(pulse pressure) .times. 100 (%); (LVRWR) = (late peak left ventricular systolic pressure - left

ventricular pressure at anacrotic **notch**)/(late peak left ventricular systolic pressure) .times. 100 (%). There was no statistical difference in the mean ages of patients in the three groups and the mean systolic and diastolic aortic pressures of them. AoRWR was 40.7 .+-. 11.0 (mean .+-. 1 SD) % in the MI group, 36.6 .+-. 9.6% in the AP group and 30.3 .+-. 11.0% in the Ot group. LVRWR was 16.7 .+-. 5.7% in the MI group, 13.3 .+-. 6.3% in the AP group and 9.4 .+-. 5.6% in the Ot group. LVRWR and AoRWR were higher in the ischemic heart disease groups than in the Ot group. LVRWR (Y) and AoRWR (X) were directly proportional, Y = 0.488X - 4.3 (r = 0.83, p < 0.001), as were the changes after angiotensin loading and nitroglycerin. .**DELTA**.LVEDP/.**DELTA**.LVRWR was high in the MI patients who received angiotensin. Nitroglycerin produced a marked decrease in LVRWR without an accompanying decrease in the aortic diastolic pressure. The ratio of the second component to the increase in the left ventricular pressure is considered to be a useful index of the excessive left ventricular afterload.

SO J TOKYO MED COLL, (1987) 45 (2), 256-270.
CODEN: TIDZAH. ISSN: 0040-8905.

AB Arterial and left ventricular systolic pressure are divided into two components by the anacrotic **notch**. The first component is mainly caused by the left ventricular ejection and the second component by the peripheral reflection wave.. . . second component of the left ventricular pressure and investigate the changes after an intravenous injection of angiotensin and a sublingual **administration** of nitroglycerin. Forty-nine patients, 18 with myocardial infarction (MI group), 20 with angina pectoris (AP group) and 11 others (Ot. . . micromanometer-tipped catheter (Miller-PC-484A) in the subjects' normal conditions and after an intravenous injection of 2.5 .mu.g angiotensin and a sublingual **administration** of 0.3 mg nitroglycerin. Aortic reflection wave ratio (AoRWR) and left ventricular reflection wave ratio (LVRWR) were expressed as follows: (AoRWR) = (late peak aortic systolic pressure-pressure at anacrotic **notch**)/(pulse pressure) .times. 100 (%); (LVRWR) = (late peak left ventricular systolic pressure - left ventricular pressure at anacrotic **notch**)/(late peak left ventricular systolic pressure) .times. 100 (%). There was no statistical difference in the mean ages of patients in. . . Y = 0.488X - 4.3 (r = 0.83, p < 0.001), as were the changes after angiotensin loading and nitroglycerin. .**DELTA**.LVEDP/.**DELTA**.LVRWR was high in the MI patients who received angiotensin. Nitroglycerin produced a marked decrease in LVRWR without an accompanying decrease. . .

=> dis his

(FILE 'HOME' ENTERED AT 15:37:34 ON 20 FEB 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 15:46:02 ON 20 FEB 2002

```
L1          851 S NOTCH (2N) LIGAND?
L2          337 S L1 AND PD<19990405
L3            0 S L2 (10N) ADMINIST?
L4            0 S L2 (P) ADMINIST?
L5        29095 S NOTCH
L6         2162 S L5 AND (SERRATE OR DELTA)
L7          763 S L6 AND RECEPTOR?
L8            0 S L7 AND ADMINISTR?
L9            0 S L7 AND ADMINIST?
L10           0 S L1 AND ADMINIST?
L11         268 S L5 AND ADMINIST?
L12         148 S L11 AND PD<19990504
L13         111 DUP REM L12 (37 DUPLICATES REMOVED)
L14           4 S L13 AND (DELTA OR SERRATE)

=> s l13 not (EEG or EKG or ventricul?)
L15          90 L13 NOT (EEG OR EKG OR VENTRICUL?)

=> dis l15 1-90 ibib abs kwic

L15  ANSWER 1 OF 90  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        1999:413982  CAPLUS
DOCUMENT NUMBER:         131:196429
TITLE:                   Acute microvascular response to photodynamic therapy
                         with mono-L-aspartyl chlorin e6 and a diode laser:
                         observation under modified operation microscope
AUTHOR(S):               Shibuya, Hiroshi; Aizawa, Katsuo; Okunaka, Tetsuya;
                         Konaka, Chimori; Saito, Kouichi; Kato, Harubumi
CORPORATE SOURCE:        Dep. Surgery, Tokyo Medical Univ., Japan
SOURCE:                  Tokyo Ika Daigaku Zasshi (1999), 57(2),
                         136-144
                         CODEN: TIDZAH; ISSN: 0040-8905
PUBLISHER:               Tokyo Ika Daigaku Igakkai
DOCUMENT TYPE:           Journal
LANGUAGE:                English
```

AB Microvascular change has been recently identified as an important factor of photodynamic therapy (PDT). Three expts. were performed to investigate this phenomenon. Two groups of mice bearing Meth-A tumor were treated with 664 nm light (100 J/cm2, 100 mW/cm2). Five (group 1) or 20.0 mg/kg (group 2) of mono-L-aspartyl chlorin e6 (NPe6) was **administered** to these mice 2 or 24 h before light exposure, resp. Tumor response was more pronounced in group 1 (tumor cure ratio was 80% vs. 25%, p < 0.05). The concn. of photosensitizer in tumors or in plasma was measured by HPLC 2 h and 24 h after **administration** of NPe6. The values of the NPe6 in tumor were similar in both groups, however, the level in plasma in group 2 was below threshold level as opposed to 2.33 +/- 0.97 .mu.g/mL in group 1. Tumor specimens obtained after PDT were examd. by phosphotungstic acid hematoxylin (PTAH) staining. Some pos. areas were detected in tumor vessels. All hemokinetic changes during or after PDT could be obsd. continuously using the improved microscope, which has a special **notch** filter preventing the passage of emission laser light. Microvascular changes were dominated by the appearance of emboli, which seemed to be platelet aggregation contg. fibrin.

```
REFERENCE COUNT:         21    THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
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SO Tokyo Ika Daigaku Zasshi (1999), 57(2), 136-144
CODEN: TIDZAH; ISSN: 0040-8905

AB Microvascular change has been recently identified as an important factor of photodynamic therapy (PDT). Three expts. were performed to investigate this phenomenon. Two groups of mice bearing Meth-A tumor were treated with 664 nm light (100 J/cm2, 100 mW/cm2). Five (group 1) or 20.0 mg/kg (group 2) of mono-L-aspartyl chlorin e6 (NPe6) was **administered** to these mice 2 or 24 h before light exposure, resp. Tumor response was more pronounced in group 1 (tumor cure ratio was 80% vs. 25%, p < 0.05). The concn. of photosensitizer in tumors or in plasma was measured by HPLC 2 h and 24 h after **administration** of NPe6. The values of the

NPe6 in tumor were similar in both groups, however, the level in plasma in group 2 was below threshold level as opposed to 2.33 +/- 0.97 .mu.g/mL in group 1. Tumor specimens obtained after PDT were examd. by phosphotungstic acid hematoxylin (PTAH) staining. Some pos. areas were detected in tumor vessels. All hemokinetic changes during or after PDT could be obsd. continuously using the improved microscope, which has a special **notch** filter preventing the passage of emission laser light. Microvascular changes were dominated by the appearance of emboli, which seemed to be platelet aggregation contg. fibrin.

L15 ANSWER 2 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:369404 CAPLUS
DOCUMENT NUMBER: 131:126639
TITLE: Concurrent teratogenic and mutagenic action of 2-methoxyethanol in Drosophila melanogaster larvae resulted in similar phenotypes: close resemblance to directed mutations
AUTHOR(S): Eisses, Karel Th.
CORPORATE SOURCE: Biochemical Institute, University of Oslo, Norway
SOURCE: Teratog., Carcinog., Mutagen. (**1999**), 19(3), 183-204
CODEN: TCMUD8; ISSN: 0270-3211
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Early third instar larvae of wild-type Drosophila melanogaster were transferred to medium supplemented with 2-methoxyethanol (2-ME) or ethylene glycol monomethyl ether. 2-ME produced terata in adult flies as wing **notches** and duplications of macrochaetae similar to feeding with methoxyacetic acid (MAA), the oxidn. product of 2-ME. Larval feeding with 2-ME also affected the fertility of both females and males. 2-ME or more likely its intermediate oxidn. product, methoxyacetaldehyde (MAALD), concurrently generated mutations in the premeiotic stages of the oocytes in the early third instar larvae. The mutagenicity of 2-ME has been confirmed in subsequent small scale expts. The mutation frequency ranged from 4.times.10-4 to 1.times.10-2. Although terata were not supposed to be heritable, 1.1 to 8.7% of the affected females produced offspring with phenotypic similarity to the female parent. This phenomenon looked like a classical example of inheritance of an acquired character. The question is addressed why a **Notch**-like phenocopy, generated by larval 2-ME treatment, could bring forth **Notch** and rudimentary mutants in particular. **Administration** of 2-ME to larvae, contg. the highly active alc. dehydrogenase variant ADH-71k, exposed the mitotic germ cells and the mitotic somatic cells of the imaginal disks simultaneously to the mutagen MAALD and the teratogen MAA, resp. The chances for specific gene mutations, though non-adaptive, were likely increased by a feedback mechanism: gene-products that were inhibited or disturbed by the teratogen demanded increased transcription of their encoding genes. Transcribed genes are more susceptible to mutagens.
REFERENCE COUNT: 130 THERE ARE 130 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Teratog., Carcinog., Mutagen. (**1999**), 19(3), 183-204
CODEN: TCMUD8; ISSN: 0270-3211
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L15 ANSWER 3 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:434652 CAPLUS
DOCUMENT NUMBER: 129:215170
TITLE: Effects of dopaminergic drugs, occlusal disharmonies, and chronic stress on non-functional masticatory activity in the rat, assessed by incisal attrition
AUTHOR(S): Gomez, F. M.; Areso, M. P.; Giralt, M. T.; Sainz, B.; Garcia-Vallejo, P.
CORPORATE SOURCE: Department of Stomatology, Faculty of Medicine and Odontology, University of the Basque Country, Vizcaya, Spain
SOURCE: J. Dent. Res. (**1998**), 77(6), 1454-1464
CODEN: JDREAF; ISSN: 0022-0345
PUBLISHER: International Association for Dental Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Observational methods and the recording of nonspecific jaw movements or masticatory muscle activity have been used to evaluate oral parafunctional movements in animal models of bruxism. In this study, the authors have used a new approach in which the non-functional masticatory activity in the rat was assessed by the measurement of incisal attrition, with the aim of investigating the role of diverse factors involved in the etiol. of bruxism. The authors quantified the attrition rate weekly by making superficial **notches** in the lower incisors and measuring the distances to the incisor edges. Repeated stimulation of the dopaminergic system with apomorphine led to an enhancement of the non-functional masticatory activity. The severity of the apomorphine-induced oral behavior was pos. correlated (rs = 0.69) with an increase in the incisal attrition rate (20.9%). Apomorphine-induced non-functional masticatory activity was strongly enhanced by the placement of an acrylic cap on both lower incisors (306%), but not by the cutting of a lower incisor. Repeated cocaine **administration** also increased the attrition rate (22.5%). However, neither chronic blockade of dopaminergic receptors with haloperidol, nor its withdrawal, modified attrition. In addn., since

emotional disturbances are considered to be causal factors of bruxism, the authors tested whether exptl. stress might accelerate tooth wear. Exposure to two different chronic stress regimes did not induce significant changes in incisal attrition. Moreover, exposure to chronic stress after the withdrawal of chronic haloperidol treatment did not alter attrition either. These results partially support the role of the central dopaminergic system in bruxism and suggest that stress, in general, may not be a relevant factor in tooth wear.

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CODEN: JDREAF; ISSN: 0022-0345

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L15 ANSWER 4 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:128771 CAPLUS
DOCUMENT NUMBER: 128:225701
TITLE: Structure-activity relation of N-alkyl tetracaine derivatives as neurolytic agents for sciatic nerve lesions
AUTHOR(S): Wang, Ging Kuo; Viadimirov, Marina; Shi, Hao; Mok, Wai Man; Thalhammer, Johann G.; Anthony, Douglas C.
CORPORATE SOURCE: Department of Anesthesia, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Anesthesiology (1998), 88(2), 417-428
CODEN: ANESAV; ISSN: 0003-3022
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB N-Bu tetracaine has local anesthetic and neurolytic properties. An injection of this drug at the rat sciatic **notch** produces rapid onset and nerve impairment lasting > 1 wk. This study aimed to elucidate the structure-activity relation of various tetracaine derivs. to design better neurolytic agents. N-alkyl tetracaine salts (n = 2-6) were synthesized, and their ability to elicit sciatic nerve impairment of sensory and motor functions in vivo was tested in rats. A single dose (0.1 mL at 37 mM) was **administered** close to the sciatic nerve at the sciatic **notch**. Regeneration was assessed morphol. in transverse sections of treated nerves. Finally, the drug potency in blocking Na+ currents was studied under voltage-clamp conditions. N-Et and N-Pr tetracaine derivs. were non-neurolytic and elicited complete sciatic nerve block lasting 3-7 h. In contrast, N-Bu, N-pentyl, and N-hexyl tetracaine derivs. were strong neurolytic agents and elicited functional impairment of sciatic nerve for > 1 wk. All derivs. were strong Na+ channel blockers, more potent than tetracaine if applied intracellularly. External drug application showed marked differences in their wash-in rate: tetracaine > N-hexyl > N-Bu > N-Et tetracaine. All derivs. were trapped within the cytoplasm and showed little washout within 7 min. When n-alkylation is 4-6, n-alkyl tetracaine appeared as a strong neurolytic agent. Neurolytic derivs. retained their local anesthetic activity and elicited rapid onset of nerve block after injection. Such derivs. are potential local anesthetic-neurolytic dual agents for chem. lesions of the sciatic nerve.

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CODEN: ANESAV; ISSN: 0003-3022

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L15 ANSWER 5 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:32017 CAPLUS
DOCUMENT NUMBER: 126:70047
TITLE: N-Butyl tetracaine as a neurolytic agent for ultralong sciatic nerve block
AUTHOR(S): Wang, G. K.; Vladimirov, M.; Quan, C.; Mok, W. M.; Thalhammer, J. G.; Anthony, D. C.
CORPORATE SOURCE: Department Anesthesia, Brigham and Women's Hospital, Boston, MA, 02115, USA
SOURCE: Anesthesiology (1996), 85(6), 1386-1394

CODEN: ANESAV; ISSN: 0003-3022
PUBLISHER: Lippincott-Raven
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Neurolytic agents such as phenol (5% to 10%) and abs. alc. have long been used clin. to destroy the pathogenic nerve regions that manifest pain. Both phenol and alc. are highly destructive to nerve fibers. However, these agents exert only weak local anesthetic effects and therefore are difficult to **administer** to alert patients without pain. This report describes a tetracaine deriv. that displays both local anesthetic and neurolytic properties. Studies with such a compd. may lead to the design of neurolytic agents that are more effective and more easily **administered** than phenol and alc. The tetracaine deriv., N-Bu tetracaine quaternary ammonium bromide, was synthesized, and its ability to elicit sciatic nerve block of sensory and motor functions in vivo was tested in rats. A single dose of 0.1 mL N-Bu tetracaine at 37 mM was injected into the sciatic **notch**. Transverse sections of treated sciatic nerves were subsequently examd. to det. the neurolytic effect of this drug. Finally, the local anesthetic properties of N-Bu tetracaine were studied in vitro; both tonic inhibition and use-dependent inhibition of Na+ currents in neuronal GH3 cells were characterized under whole-cell voltage-clamp conditions. The results showed that N-Bu tetracaine at 37 mM (equiv. to 1.11% tetracaine-hydrochloric acid concn.) elicited prolonged sciatic nerve block of the withdrawal response to noxious pinch in rats for more than 2 wk. The withdrawal response was fully restored after 9 wk. Parallel to sensory block, motor functions of the hind legs were similarly blocked by this drug. Morphol. examns. 3 and 5 wk after a single injection of drug revealed degeneration of many sciatic nerve fibers, consistent with the results of functional tests. Finally, N-Bu tetracaine was found to be a potent Na+ channel blocker in vitro. It produced strong tonic and use-dependent inhibition of Na+ currents with a potency comparable to that of tetracaine. In conclusion, a single injection of N-Bu tetracaine produces ultralong sciatic nerve block in rats. This compd. possesses both local anesthetic and neurolytic properties and may prove useful as a neurolytic agent in pain management.
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CODEN: ANESAV; ISSN: 0003-3022
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L15 ANSWER 6 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:345477 CAPLUS
DOCUMENT NUMBER: 122:193688
TITLE: Impact toughness evaluation of cold-service ethylene plant vessels
AUTHOR(S): Dugas, John R.; Damin, Dean G.; Aller, John E.; Williams, David
CORPORATE SOURCE: E.I. DuPont de Nemours & Company, USA
SOURCE: Proc. - Ethylene Prod. Conf. (**1994**), Volume Date 1993, 2, 1-17
CODEN: PEPCE8; ISSN: 1066-1557
DOCUMENT TYPE: Journal
LANGUAGE: English
AB After 25 + years of satisfactory operation, a potential problem with the cold-service vessels of Du Pont Sabine River Works (SRW) Ethylene Plant was recognized. A program was instituted to identify, evaluate and subsequently correct low temp. ductility problems with vessels operating below 0.degree. (32.degree.F) that could result in a catastrophic failure. The integrity of the suspected vessels at low temps. was evaluated using field metallog. and replication techniques, fracture mechanics, Charpy V-**notch** impact testing and results from a hazards and operability (HAZOP) study. During the evaluation period and the time required to bring about the permanent soln., short-term training and **administrative** controls were implemented. As a result, 10 pieces of equipment were replaced and 12 pieces of equipment were recommended to be replaced at considerable expense.
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CODEN: PEPCE8; ISSN: 1066-1557
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L15 ANSWER 7 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:298835 CAPLUS

DOCUMENT NUMBER: 122:308471
TITLE: Differences in teratogenic and toxic properties of alcohol dehydrogenase inhibitors pyrazole and 4-methylpyrazole in Drosophila melanogaster: II. ADH allozymes in an isogenic background
AUTHOR(S): Eisses, Karel Th.
CORPORATE SOURCE: Dep. Plant Ecol. Evol. Biol., Utrecht Univ., Neth.
SOURCE: Teratog., Carcinog., Mutagen. (**1994**), 14(6), 291-302
CODEN: TCMUD8; ISSN: 0270-3211
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pyrazole and 4-methylpyrazole (4-MP) are in vivo and in vitro inhibitors of alc. dehydrogenase activity in mammals. The fruitfly Drosophila melanogaster has been used to demonstrate the influence of genetic variation in alc. dehydrogenase alleles of the results of larval treatment with pyrazole and 4-MP. Genetic polymorphism of organisms involved in expts. with teratogenic and toxic agents is not often considered. **Administration** of pyrazole to larvae of isogenic D. melanogaster strains, differing mainly in their Adh alleles, caused large **Notch** -like teratogenic aberration, macrochaetae multiplication, and pupal mortality. The level of teratogenicity and developmental-toxicity of pyrazole was both concn. and Adh-genotype-dependent. The strain with the highest ADH activity showed smaller effects after the treatments with the two concns. used. 4-MP does not cause morphol. aberrations, although treatment of larvae with an isogenic background caused a high pupal mortality due to non-differentiated material in the pupal case.

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CODEN: TCMUD8; ISSN: 0270-3211
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L15 ANSWER 8 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:244779 CAPLUS
TITLE: Histological evaluation of bone-cement interface affected by polyethylene particles in rabbit knee
AUTHOR(S): Ohashi, H.; Kobayashi, A.; Yoshida, K.; Yutani, Y.; Yamano, Y.; Oonishi, H.; Iwaki, H.
CORPORATE SOURCE: Dept. Orthopaedic Surgery, Osaka City Univ. Med. School, Osaka, 545, Japan
SOURCE: J. Mater. Sci.: Mater. Med. (**1994**), 5(9&10), 610-12
CODEN: JSMMEL; ISSN: 0957-4530
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To investigate the biol. process of aseptic component loosening caused by polyethylene wear debris, 9 rabbits were implanted with acrylic cement into the non-wt.-bearing intercondylar **notch** of distal femur. Six animals were **administered** the particles of polyethylene into the knee joint repeatedly for 12 wk. At the bone-cement interface, thin connective tissue was obsd., while bone sometimes existed directly next to the acrylic cement. The percentage of the length of interposed fibrous tissue against the total length of bone-cement interface was measured. The percentage was 15.8 .+-. 10.3 in the polyethylene-injected group and 8.3 .+-. 7.7 in the control group (no significance). While not significant, the amt. was greater in the polyethylene-injected group (no significance). While not significant, the amt. was greater in the polyethylene-injected group. Thus it is proposed that the polyethylene particles played a role in bone resorption and fibrous tissue formation at the bone-cement interface. In some specimens, macrophages and foreign body giant cells that surrounded the particles near the articular surface were seen to cause resorption of bone. It is supposed that this phenomenon is similar to the focal osteolysis that is sometimes obsd. around a prosthetic component.

SO J. Mater. Sci.: Mater. Med. (**1994**), 5(9&10), 610-12
CODEN: JSMMEL; ISSN: 0957-4530
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L15 ANSWER 9 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:426887 CAPLUS
DOCUMENT NUMBER: 121:26887
TITLE: Therapeutic and diagnostic methods and compositions based on **Notch** proteins and nucleic acids
INVENTOR(S): Artavanis-Tsakonas, Spyridon; Fehon, Richard Grant; Zagouras, Panayiotis; Blaumueller, Christine Marie
PATENT ASSIGNEE(S): Yale University, USA
SOURCE: PCT Int. Appl., 232 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9407474	A1	19940414	WO 1993-US9338	19930930 <--
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5786158	A	19980728	US 1993-83590	19930625 <--
EP 662827	A1	19950719	EP 1993-923752	19930930 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08502170	T2	19960312	JP 1993-509326	19930930 <--
AU 685067	B2	19980115	AU 1994-53503	19930930 <--

PRIORITY APPLN. INFO.:
US 1992-955012 A2 19920930
US 1993-83590 A2 19930625
US 1992-879038 B2 19920430
WO 1993-US9338 W 19930930

AB Therapeutic and diagnostic methods and compns. based on **Notch** proteins and nucleic acids are provided. The sequences of human **Notch** cDNA and the encoded human **Notch** protein are also disclosed. The invention provides treatment of disorders of cell fate or differentiation by **administration** of a therapeutic compd. of the invention. Such therapeutic compds. include **Notch** proteins and analogs and derivs. (including fragments) thereof, antibodies thereto, nucleic acids encoding the **Notch** proteins, analogs, or derivs., **Notch** antisense nucleic acids, as well as toporythmic proteins and derivs. which bind to or otherwise interact with **Notch** proteins, their encoding nucleic acids or antibodies. The therapeutic is **administered** to treat a cancerous condition, or to prevent progression from a pre-neoplastic or non-malignant state into a neoplastic or a malignant state.

TI Therapeutic and diagnostic methods and compositions based on **Notch** proteins and nucleic acids

PI WO 9407474 A1 **19940414**

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9407474	A1	19940414	WO 1993-US9338	19930930 <--
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5786158	A	19980728	US 1993-83590	19930625 <--
EP 662827	A1	19950719	EP 1993-923752	19930930 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08502170	T2	19960312	JP 1993-509326	19930930 <--
AU 685067	B2	19980115	AU 1994-53503	19930930 <--

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ST human **Notch** protein therapeutic; cDNA antibody human **Notch**

IT Alopecia
Cirrhosis
Keloid
Psoriasis
(**Notch** protein as diagnosistics and)

IT Gene, animal
RL: BIOL (Biological study)
(cDNA, for human **Notch** protein and Drosophila Delta protein)

IT Protein sequences
(of human **Notch** protein and Drosophila Delta protein)

IT Antibodies
RL: BIOL (Biological study)
(to human **Notch** protein, for diagnostics and therapeutics)

IT Gene, animal
RL: BIOL (Biological study)
(Serrate, protein of, **Notch** protein as therapeutics in relation to)

IT Uterus, neoplasm
(cervix, treatment and diagnosis of, **Notch** protein as diagnosistics and)

IT Neoplasm inhibitors
(colon, **Notch** protein as diagnosistics and)

IT Intestine, neoplasm
(colon, inhibitors, **Notch** protein as diagnosistics and)

IT Deoxyribonucleic acid sequences
(complementary, for human **Notch** protein and Drosophila Delta protein)

IT Deoxyribonucleic acids
RL: BIOL (Biological study)
(complementary, antisense, of human **Notch** gene, for diagnostics and therapeutics)

IT Proteins, specific or class
RL: BIOL (Biological study)
(gene Delta, **Notch** protein as therapeutics in relation to)

IT Lung, neoplasm
(inhibitors, **Notch** protein as diagnosistics and)

IT Neoplasm inhibitors
(lung, **Notch** protein as diagnosistics and)

IT Neoplasm inhibitors
(mammary gland, **Notch** protein as diagnosistics and)

IT Neoplasm inhibitors
(melanoma, **Notch** protein as diagnosistics and)

IT Antibodies
RL: BIOL (Biological study)
(monoclonal, to human **Notch** protein, for diagnostics and therapeutics)

IT Mammary gland
(neoplasm, inhibitors, **Notch** protein as diagnosistics and)

IT Testis, neoplasm
(seminoma, treatment and diagnosis of, **Notch** protein as diagnosistics and)

IT 146636-19-3, **Notch** protein fragment (Drosophila)
RL: BIOL (Biological study)
(human **Notch** protein homologous to, as therapeutics)
IT 146636-08-0, DNA (human clone hN2k **Notch** protein fragment encoding cDNA) 146636-13-7, DNA (human clone hN2k **Notch** protein fragment encoding cDNA) 156067-43-5 156067-44-6 156067-45-7
RL: PRP (Properties)
(nucleotide sequence of, therapeutics contg. protein encoded by)

L15 ANSWER 10 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:401286 CAPLUS
DOCUMENT NUMBER: 121:1286
TITLE: Effects of the anabolic steroid nandrolone phenylpropionate on craniofacial growth in rats
AUTHOR(S): Noda, Kazunobu; Chang, Hong-Po; Takahashi, Ichiro; Kinoshita, Zennosuke; Kawamoto, Tatsuo
CORPORATE SOURCE: Dep. Orthod., Osaka Dent. Univ., Osaka, 540, Japan
SOURCE: J. Morphol. (**1994**), 220(1), 25-33
CODEN: JOMOAT; ISSN: 0362-2525
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Primary testosterone and its derivs. are anabolic steroids used in the treatment of osteoporosis and Turner syndrome. They also enhance fast-twitch muscle wt. in female rats. The present study examines the effect of an anabolic steroid on craniofacial growth and development in rats. Five-week-old female Sprague-Dawley rats (125) were divided into exptl. and control groups. The exptl. group was injected s.c. with 1 mg nandrolone phenylpropionate in the interscapular region on alternate days, whereas those in the control group were injected with a vehicle, rachis oil. Rats were sacrificed at 60 and 120 days of age. Cephalometric anal. of soft x-ray cephalograms showed that chronic **administration** of the anabolic steroid, nandrolone phenylpropionate, resulted in: (1) about a 20% increase in body wt., (2) an increase in total skull length, (3) elongation of the maxillary and mandibular incisors, (4) an increase in the depth of the antegonial **notch**, and (5) downward-forward growth of the viscerocranium against the neurocranium. These results suggest that nandrolone phenylpropionate may accelerate craniofacial growth and/or induce high functional activity of the masticatory muscles in female rats.
SO J. Morphol. (**1994**), 220(1), 25-33
CODEN: JOMOAT; ISSN: 0362-2525
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L15 ANSWER 11 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:143600 CAPLUS
DOCUMENT NUMBER: 116:143600
TITLE: Effects of adrenoceptor agonists and antagonists on cardiovascular functional parameters in rats
AUTHOR(S): Young, M. S.; Lin, K. W.; Lin, M. T.
CORPORATE SOURCE: Dep. Electr. Eng., Natl. Cheng-Kung Univ., Tainan, Taiwan
SOURCE: Pharmacology (**1992**), 44(4), 225-36
CODEN: PHMGBN; ISSN: 0031-7012
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of i.v. **administration** of adrenoceptor agonists and antagonists on electrocardiog. or blood pressure (BP) functional parameters were assessed in urethane-anesthetized rats. The responses of cardiovascular functional parameters produced by these drugs included as follows: (1) isoproterenol decreased the duration of a whole BP cycle (Wd), duration of the diastolic wave (Dd), peak amplitude of the systolic wave (SYa), amplitude of the diastolic **notch** (DNa), amplitude of the diastolic wave (DWa), pulse pressure (dp) and mean arterial pressure (mp) but increased the heart rate (HR) accompanied by prolonged R-R (RR) or P-P interval (PP); (2) propranolol decreased Sya, DNa, dp, mp, HR, the amplitude of the P wave (Pa) and amplitude of the S wave (Sa) but increased the duration of the QRS wave, P-R interval, duration of the R wave (Rd) and duration of the P wave (Pd); (3) adrenaline decreased HR (accompanied by prolonged RR and PP), Rd, Pa and amplitude of the T wave (Ta) but increased Pd, Wd, Dd, DNA, the time interval between aortic valve opening and closure (Dw), dp, mp, amplitude of the Q wave and amplitude of the R wave (Ra); (4) noradrenaline decreased HR (accompanied by prolonged RR and PP) and Pa but increased Wd, Pd, SYa, DNa, Dw, dp, mp, Ra and Ta; (5) phenylephrine decreased HR (accompanied by prolonged RR and PP) and Pa but increased Wd, Dd, DNa, mp and Ra; (6) phentolamine decreased SYa, DNa, DWa, Dw, dp and mp. This study illustrates the utility of the automated ECG (ECG) and BP anal. system for investigation of adrenoceptor agonists and antagonists. The use of this methodol. not only reproduced most of cardiovascular functional parameter effects produced by these drugs using the conventional methodol. but also realizes some new information about the drug-induced ECG or BP waveform effects.
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CODEN: PHMGBN; ISSN: 0031-7012
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(accompanied by prolonged RR and PP), Rd, Pa and amplitude of the T wave (Ta) but increased Pd, Wd, Dd, DNA, the time interval between aortic valve opening and closure (Dw), dp, mp, amplitude of the Q wave and amplitude of the R wave (Ra); (4) noradrenaline decreased HR (accompanied by prolonged RR and PP) and Pa but increased Wd, Pd, SYa, DNa, Dw, dp, mp, Ra and Ta; (5) phenylephrine decreased HR (accompanied by prolonged RR and PP) and Pa but increased Wd, Dd, DNa, mp and Ra; (6) phentolamine decreased SYa, DNa, DWa, Dw, dp and mp. This study illustrates the utility of the automated ECG (ECG) and BP anal. system for investigation of adrenoceptor agonists and antagonists. The use of this methodol. not only reproduced most of cardiovascular functional parameter effects produced by these drugs using the conventional methodol. but also realizes some new information about the drug-induced ECG or BP waveform effects.

L15 ANSWER 12 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:53030 CAPLUS
DOCUMENT NUMBER: 116:53030
TITLE: Evaluation of Drosophila for screening developmental toxicants: test results with eighteen chemicals and presentation of a new Drosophila bioassay
AUTHOR(S): Lynch, Dennis W.; Schuler, Ronald L.; Hood, Ronald D.; Davis, D. Gale
CORPORATE SOURCE: Div. Biomed. Behav. Sci., Natl. Inst. Occup. Saf. Health, Cincinnati, OH, 45226-1998, USA
SOURCE: Teratog., Carcinog., Mutagen. (1991), 11(3), 147-73
CODEN: TCMUD8; ISSN: 0270-3211
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective of this study was to generate a comprehensive data set of chem. induced malformations in Drosophila using a detailed morphol. examn. of the entire fly (phase one). These data were analyzed, in blind, with the goal of developing a standardized set of criteria which could be used in a new, rapid, and economical Drosophila bioassay useful in the preliminary screening for potential developmental toxicants. After 32 chems. were tested, formalized criteria were developed to form the basis of a new Drosophila bioassay. These critera were then applied to the data from the same 32 chems. (phase two). The data from only 18 of these chems. met all requirements for evaluation, e.g., statistical significance, min. fly nos., sufficient challenge concn. **administered**, etc. In the new bioassay, rather than the detailed and time-consuming examn. of the entire fly for a multitude of morphol. defects, only 2 specific anatomical sites are examd. These sites are the humeral bristle and the wing blade, with focus placed on 2 structural defects-a bent bristle and a **notch** in the wing. These defects were the only 2 external malformations among the multitude of defects obsd. in flies treated in the 1st phase with the 32 chems. which demonstrated the following characteristics: 1) a consistent concn.-response in flies treated with a variety of developmental toxicants; 2) a lack of response with most presumptive nondevelopmental toxicants; and 3) consistently low-background incidences in control flies. In both phases, developing Drosophila were exposed to the test agents from the egg through 3 larval stages by incorporating a range of concns. of each chem. into the culture medium. Emerging adults were examd. for an array of defects as part of a detailed morphol. examn. in the 1st phase, including bent bristles and wing **notches**. In the 2nd phase, only bent bristle and wing **notch** data were evaluated. The incidences of bent humeral bristles and wing **notches** from flies exposed to each of the 18 chems. were compared with those fo concurrent controls. Of the 18 chems. that could be evaluated using the new bioassay, 13 were known developmental toxicants while the remaining 5 were presumptive neg. agents. Ten of the 13 mammalian developmental toxicants were correctly identified with this test (false neg. rate of 23%). Four of 5 apparent nondevelopmental toxicants were correctly identified for a false pos. rate of 20%. The sensitivity of the bioassay was 77% (10 of 13 known developmental toxicants accurately detected); the specificity was 80% (4 of 5 neg. compds. accurately detected); and the overall accuracy was 78% (14 of 18 chems. accurately detected).
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CODEN: TCMUD8; ISSN: 0270-3211
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L15 ANSWER 13 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:225349 CAPLUS
DOCUMENT NUMBER: 110:225349

TITLE: Toxic effects of triethyldodecylammonium bromide (TEA-C12) on myelinated nerve fibers and blood-nerve barrier in the mouse
AUTHOR(S): Seitz, R. J.; Lipfert, P.; Willrich, A.; Himmelmann, F.
CORPORATE SOURCE: Dep. Neurol., Univ. Hosp., Duesseldorf, D-4000, Fed. Rep. Ger.
SOURCE: Exp. Brain Res. (1989), 74(2), 293-302
CODEN: EXBRAP; ISSN: 0014-4819
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The blocking effect of TEA-C12, applied locally to the sciatic nerve, was studied in 28 adult mice. Clin. parameters, electrophysiol. recordings of muscle action potentials evoked by stimulation at the sciatic **notch**, and morphol. aspects are presented. The minimal blocking concn. and half the minimal blocking concn. induce flaccid paresis of the treated hind-limb. There was a complete, long-lasting nerve conduction block due to Wallerian degeneration of the myelinated nerve fibers. In contrast, pain sensation was abolished only on day 4 after application of the minimal blocking concn., but was preserved during the rest of the time that nerve conduction block was obsd. Recovery of nerve conduction was characterized electrophysiol. by occurrence of minute polyphasic regeneration potentials between day 18 and 21, clin. by advanced restitution of muscle force on day 64, and morphol. by nerve regeneration. TEA-C12 also induced a disturbance of the blood-nerve barrier, demonstrated using an i.p. **administered** biotinylated IgG tracer in the endoneurial space.
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CODEN: EXBRAP; ISSN: 0014-4819
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L15 ANSWER 14 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:64569 CAPLUS
DOCUMENT NUMBER: 106:64569
TITLE: Induction of **Notch**-like phenocopies by methoxyacetate dependent on alcohol dehydrogenase allozymes of Drosophila melanogaster
AUTHOR(S): Eisses, Karel T.; Heinstra, Pieter W. H.; Scharloo, Willem; Thoerig, George E. W.
CORPORATE SOURCE: Dep. Popul. Evol. Biol., Rijksuniv. Utrecht, Utrecht, 3584 CH, Neth.
SOURCE: Comp. Biochem. Physiol., B: Comp. Biochem. (1986), 85B(4), 759-65
CODEN: CBPBB8; ISSN: 0305-0491
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Third-instar larvae of 2 wild-type strains of D. melanogaster, homozygous for the alc. dehydrogenase (ADH; EC 1.1.1.1) alloenzymes ADH71k and ADHF from alleles Adh71k and AdhF, resp., were exposed to methoxyacetate, an inhibitor of sarcosine dehydrogenase (I). The 2 strains showed a different **Notch** gene mutation-like phenocopy frequency. This is explained as a consequence of the different oxidn. rates of sarcosine by ADH71k and ADHF. Inhibition of ADH activity in vivo by acetone, before the **administration** of methoxyacetate, enhanced in both strains differentially the frequency of wing **notches** and mortality. Then the phenocopy frequency in the Adh71k strain almost equalled that of the AdhF strain. The activity of I is controlled by the **Notch** locus. Activity of I is lowered by **Notch** mutations and methoxyacetate, whereas at the same time they do not affect the activity of ADH. Apparently, ADH71k forms a bypass for sarcosine oxidn., when in vivo I is reduced either by artificial in vivo inhibition or by a mutation. This explains also the fixation of the Adh71k allele in stocks with **Notch** mutants of D. melanogaster.
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ST alc dehydrogenase alloenzyme methoxyacetate Drosophila; **Notch** phenocopy methoxyacetate alc dehydrogenase
IT Drosophila melanogaster
(alc. dehydrogenase alloenzymes of, **Notch**-like phenocopy induction by sarcosine dehydrogenase inhibition dependent on)
IT Gene and Genetic element, animal
RL: BIOL (Biological study)
(Adh, for alc. dehydrogenase alloenzyme, of Drosophila, **Notch**-like phenocopy induction by sarcosine dehydrogenase in relation to)
IT Gene and Genetic element, animal
RL: BIOL (Biological study)
(**Notch**, mutations of, of Drosophila, alc. dehydrogenase alloenzymes and sarcosine dehydrogenase in relation to)

IT 9031-72-5
RL: BIOL (Biological study)
(alloenzymes of, of Drosophila, **Notch**-like phenocopy induction by sarcosine dehydrogenase inhibition dependent on)
IT 37228-65-2, Sarcosine dehydrogenase
RL: BIOL (Biological study)
(methoxyacetate inhibition of, **Notch**-like phenocopy induction by, in Drosophila, alc. dehydrogenase alloenzymes in relation to)
IT 20758-58-1, Methoxyacetate
RL: BIOL (Biological study)
(**Notch**-like phenocopy induction by, in Drosophila, alc. dehydrogenase alloenzyme dependency in)

L15 ANSWER 15 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:61144 CAPLUS
DOCUMENT NUMBER: 106:61144
TITLE: Effects of repeated bupivacaine **administration** on sciatic nerve and surrounding muscle tissue in rats
AUTHOR(S): Kytta, J.; Heinonen, E.; Rosenberg, P. H.; Wahlstroem, T.; Gripenberg, J.; Huopaniemi, T.
CORPORATE SOURCE: Dep. Anaesthesiol., Helsinki Univ. Cent. Hosp., Helsinki, Finland
SOURCE: Acta Anaesthesiol. Scand. (**1986**), 30(8), 625-9
CODEN: AANEAB; ISSN: 0001-5172
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of repeated **administration** of 0.5% bupivacaine [2180-92-9] or saline into the sciatic **notch** of rats were studied by light microscopy, electron microscopy and a neurophysiol. technique. Severe myositis, including local necrosis, developed in 6 of 12 rats treated twice daily with 1 mL bupivacaine for either 3 or 7 days. A 3-h infusion of 1.5% bupivacaine resulted in minor injury to muscle tissue. A marked degree of disruption and vacuolization of myelin sheaths was evident in nerves exposed to bupivacaine for 3 days. Lymphocyte accumulation was confined to the area surrounding the nervous tissue in 7 of 10 of the prepns. from rats treated for 3 days or by a 3-h infusion. No histol. changes were detected in nerve and muscle tissue from the opposite extremity exposed to saline. After a recovery period of 3 wk, no differences in the nerve or muscle histol. were seen between samples from bupivacaine- or saline-treated animals. The amplitude of the compd. action potential of sciatic nerves was, however, significantly lower after bupivacaine treatment (7 days, 1 mL twice daily). Thus, impaired function may continue despite the lack of histol. intraneural injury.
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L15 ANSWER 16 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:96650 CAPLUS
DOCUMENT NUMBER: 100:96650
TITLE: Effect of tubocurarine and decamethonium on voluntary muscle contractions in man
AUTHOR(S): Secher, N. H.; Rube, N.; Secher, O.
CORPORATE SOURCE: Dep. K, Frederiksberg Hosp., Copenhagen, Den.
SOURCE: Acta Anaesthesiol. Scand. (**1983**), 27(6), 480-3
CODEN: AANEAB; ISSN: 0001-5172
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Six healthy, young male subjects performed repeated brisk maximal voluntary muscle contractions (MVC) with the knee and hip extensors. Three MVCs were performed every minute. On sep. days decamethonium bromide [541-22-0] (0.03 mg/kg) and tubocurarine chloride [57-94-3] 0.01 mg/kg were **administered** i.v. during repeated MVCs. While ordinary MVCs showed a slow rate of rise of tension over approx. 1 s, brisk MVCs showed a steep rate of rise of tension and a biphasic configuration appeared, as a **notch** was seen 370-480 ms after the initiation of the contraction curve. An arbitrary straight line was drawn connecting the starting point of the contraction curve and the **notch**. The tension time integral to the left and above this line (.alpha. component), resp. to the right and below the line (.beta. component) was measured during the first 600 ms of the contraction. Tubocurarine affected the .beta. component until it was 70% reduced. With further curarization, the remainder of the .beta. component was reduced together with the .alpha. component. Decamethonium, in contrast, affected the .alpha. component together with 30% of the .beta. component. Thereafter, the rest of the .beta. component was increasingly affected. The results suggest that the isometric mechanogram is composed of a phasically active component with a high innervation threshold primarily sensitive to decamethonium, and a tonically active component with a lower innervation threshold, and primarily sensitive to tubocurarine.
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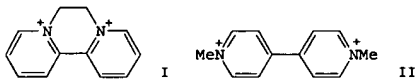
L15 ANSWER 17 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:465824 CAPLUS
DOCUMENT NUMBER: 99:65824
TITLE: Increase in the content of resin in the wood of Scotch pine (Pinus sylvestris L.) by diquat and paraquat injections
AUTHOR(S): Kudela, Michael; Mentberger, Jaroslav
CORPORATE SOURCE: Ustav Aplikovane Ekol. Ekotech., Kostelec nad Cernymi lesy, 281 53, Czech.
SOURCE: Lesnictvi (1983), 29(5), 407-22
CODEN: LSNCAE; ISSN: 0024-1105
DOCUMENT TYPE: Journal
LANGUAGE: Czech
GI



I II

AB Injections of 0.10-0.56 g Reglone (I; diquat) [85-00-7] or Gramoxone (II; paraquat) [1910-42-5]/tree into **notches** or bores made 0.5 m above ground in 43-111-yr-old pines increased the resin content by 98-306% in the bottom 4-m section of the trunk. The resin content decreased from the I or II **administration** site upwards. The treatment effectiveness depended on weather. The effectiveness was higher in 43-8- than in 111-yr-old pines. The most intensive prodn. of resin was obsd. from late Apr. to mid-June after the spring applications of the chems.; if applied in July, the greatest prodn. was found in the subsequent vegetative period. The increased resin prodn. was still recorded in the 3rd growing season in 43-yr-old pines. The chem. treated trees were not more susceptible than the controls to infestation by insects living under the bark.
SO Lesnictvi (1983), 29(5), 407-22
CODEN: LSNCAE; ISSN: 0024-1105
AB Injections of 0.10-0.56 g Reglone (I; diquat) [85-00-7] or Gramoxone (II; paraquat) [1910-42-5]/tree into **notches** or bores made 0.5 m above ground in 43-111-yr-old pines increased the resin content by 98-306% in the bottom 4-m section of the trunk. The resin content decreased from the I or II **administration** site upwards. The treatment effectiveness depended on weather. The effectiveness was higher in 43-8- than in 111-yr-old pines. The most intensive prodn. of resin was obsd. from late Apr. to mid-June after the spring applications of the chems.; if applied in July, the greatest prodn. was found in the subsequent vegetative period. The increased resin prodn. was still recorded in the 3rd growing season in 43-yr-old pines. The chem. treated trees were not more susceptible than the controls to infestation by insects living under the bark.

L15 ANSWER 18 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:199415 CAPLUS
DOCUMENT NUMBER: 94:199415
TITLE: A fractographic study of a thick wall pressure vessel failure
AUTHOR(S): Canonico, D. A.; Crouse, R. S.; Henson, T. J.
CORPORATE SOURCE: Oak Ridge Natl. Lab., Oak Ridge, TN, 37830, USA
SOURCE: Microstruct. Sci. (1980), 8, 283-94
CODEN: MSSCDJ; ISSN: 0361-1213
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A Heavy Section Steel Technol. (HSST) Program sponsored by the Nuclear Regulatory Commission (NCR) and **administered** by the Oak Ridge National Lab. (ORNL) is concerned with the safety and reliability of nuclear pressure vessels. Some of the testing involves pressurizing to failure simulated pressure vessels contg. large fatigue sharpened flaws. The vessel described here is identified as Intermediate Test Vessel 1 (ITV-1) and was fabricated from SA508, Class 2 Steel [37188-11-7]. It was tested to failure at 54.degree.. The gross failure appeared to be a brittle factor although accompanied by a measured strain of 0.9%. Seven regions of the fracture were examd. in detail, and the obsd. surfaces were compared to Charpy V-**notch** specimens of SA508, Class 2 steel broken at temps. above and below the ductile to brittle transition temp. Three samples from the vessel were taken in the region around the fatigue **notch** and 4 from areas well removed from the **notch**. All these were carefully examd. both optically and by SEM. Early crack extension was by ductile mode until a large flaw .apprx.500 mm long by 83 mm wide was developed. At this point, this vessel could no longer contain the internal pressure and final rupture was by brittle fracture.
SO Microstruct. Sci. (1980), 8, 283-94
CODEN: MSSCDJ; ISSN: 0361-1213
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the internal pressure and final rupture was by brittle fracture.

L15 ANSWER 19 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:401437 CAPLUS
DOCUMENT NUMBER: 93:1437
TITLE: Aminopyridines mimic mutant Drosophila developmental defects
AUTHOR(S): Salkoff, Lawrence; Kelly, Leonard
CORPORATE SOURCE: Dep. Genet., Univ. California, Berkeley, CA, 94720, USA
SOURCE: Comp. Biochem. Physiol. C (1980), 65C(1), 59-63
CODEN: CBPCBB; ISSN: 0306-4492
DOCUMENT TYPE: Journal
LANGUAGE: English
AB When **administered** for .gtoreq.15 h to third-instar larvae of D. melanogaster, 2- [504-29-0] and 3-aminopyridine [462-08-8] induced developmental defects similar to those obsd. in shibire and **Notch** loci phenotype mutants. Thoracic, wing, leg, and eye defects were obsd. and >70 h treatment caused death. LD50 values were 8.1 and 3.1 mM for 2- and 3-aminopyridine resp. 4-Aminopyridine [504-24-5] was less toxic (LD50 10.6mM) and effected fewer developmental defects. Neuromuscular junction transmission in larvae was enhanced by the aminopyridines, probably due to K blockade in the presynaptic nerve terminal. NEt4+, which also blocks K conductance, but from the inside of neuronal membranes, did not produce developmental defects.
SO Comp. Biochem. Physiol. C (1980), 65C(1), 59-63
CODEN: CBPCBB; ISSN: 0306-4492
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L15 ANSWER 20 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1976:77589 CAPLUS
DOCUMENT NUMBER: 84:77589
TITLE: Development of the AASHTO [American Association of State Highway and Transportation Officials] fracture-toughness requirements for bridge steels
AUTHOR(S): Barsom, John M.
CORPORATE SOURCE: U. S. Steel Res., Pittsburgh, Pa., USA
SOURCE: Eng. Fract. Mech. (1975), 7(3), 605-18
CODEN: EFMEAH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects are described of temp. and strain rate on the fracture-toughness behavior of bridge steels. The test results showed the existence of a fracture-toughness transition that is an inherent material property rather than a behavior caused only by a change in the stress state. The effect of a slow loading rate, compared with impact loading rates, is to shift the fracture-toughness transition to lower temps. The magnitude of the temp. shift between slow loading (.ovrhdot..epsilon. .apprxeq.10-5d/sec) and impact loading (.ovrhdot..epsilon. .apprxeq.10/sec) decreased with increased yield strength. The fracture-toughness behavior of bridge steels under strain rates that are encountered in actual bridge (.ovrhdot..epsilon. .apprxeq.10-3/sec) is closer to slow loading than to impact loading. Relations are presented among fracture-toughness values detd. by testing fracture-mechanics-type specimens, Charpy V-**notch** (CVN) specimens, and nil-ductility-transition (NDT) specimens. Moreover, procedures are presented for using CVN impact-test results to predict KIc values at slow or at moderate loading rates such as occur in actual bridges. The predicted KIc values are shown to be close to those exptly. detd. by testing KIc specimens at various strain rates. The test results were used to develop fracture-toughness requirements for bridge steels. These toughness requirements were approved by the Federal Highway **Administration** and by the AASHTO and are mandatory requirements on all Federal-aid highway programs in the U.S.
SO Eng. Fract. Mech. (1975), 7(3), 605-18
CODEN: EFMEAH
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L15 ANSWER 21 OF 90 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1968:97921 CAPLUS
DOCUMENT NUMBER: 68:97921
TITLE: Plane strain fracture toughness evaluation of 18 percent nickel maragin welded steel plate
AUTHOR(S): Smith, Herschel LeRoy
CORPORATE SOURCE: Naval Res. Lab., Washington, D. C., USA
SOURCE: Proc. Int. Symp. Space Technol. Sci., 6th (1966), Meeting Date 1965, 439-48
CODEN: 19WRA7
DOCUMENT TYPE: Conference
LANGUAGE: English

AB A large no. of plane strain fracture toughness measurements were made on 200 kpsi. and 250 kpsi. grades for the National Aeronatics and Space **Administration**. The 3-point **notch** bend test was used on various types of welds and zones within the welds of 3/4-inch material. Attempts were made to correlate microstructure with fracture toughness.
SO Proc. Int. Symp. Space Technol. Sci., 6th (**1966**), Meeting Date 1965, 439-48
CODEN: 19WRA7
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L15 ANSWER 22 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000001746 EMBASE
TITLE: Photoplethysmographic assessment of pulse wave reflection: Blunted response to endothelium-dependent beta2-adrenergic vasodilation in type II diabetes mellitus.
AUTHOR: Chowienczyk P.J.; Kelly R.P.; MacCallum H.; Millasseau S.C.; Andersson T.L.G.; Gosling R.G.; Ritter J.M.; Anggard E.E.
CORPORATE SOURCE: Dr. P.J. Chowienczyk, Department of Clinical Pharmacology, St. Thomas' Hospital, Lambeth Palace Road, London SE1 7EH, United Kingdom. p.chowienczyk@umds.ac.uk
SOURCE: Journal of the American College of Cardiology, (**1999**) 34/7 (2007-2014).
Refs: 31
ISSN: 0735-1097 CODEN: JACCDI
PUBLISHER IDENT.: S 0735-1097(99)00441-6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB OBJECTIVES: We sought to determine whether a simple index of pressure wave reflection may be derived from the digital volume pulse (DVP) and used to examine endothelium-dependent vasodilation in patients with type II diabetes mellitus. BACKGROUND: The DVP exhibits a characteristic **notch** or inflection point that can be expressed as percent maximal DVP amplitude (IP(DVP)). Nitrates lower IP(DVP), possibly by reducing pressure wave reflection. Response of IP(DVP) to endothelium-dependent vasodilators may provide a measure of endothelial function. METHODS: The DVP was recorded by photoplethysmography. Albuterol (salbutamol) and glyceryl trinitrate (GTN) were **administered** locally by brachial artery infusion or systemically. Aortic pulse wave transit time from the root of the subclavian artery to aortic bifurcation (T(Ao)) was measured by simultaneous Doppler velocimetry. RESULTS: Brachial artery infusion of drugs producing a greater than threefold increase in forearm blood flow within the infused limb was without effect on IP(DVP), whereas systemic **administration** of albuterol and GTN produced dose- dependent reductions in IP(DVP). The time between the first and second peak of the DVP correlated with T(Ao) ($r = 0.75$, $n = 20$, $p < 0.0001$). The effects of albuterol but not GTN on IP(DVP) were attenuated by N(G)-monomethyl-L-arginine. The IP(DVP) response to albuterol (400 .mu.g by inhalation) was blunted in patients with type II diabetes mellitus as compared with control subjects (fall 5.9 .+-. 1.8% vs. 11.8 .+-. 1.8%, $n = 20$, $p < 0.02$), but that to GTN (500 .mu.g sublingually) was preserved (fall 18.3 .+-. 1.2% vs. 18.6 .+-. 1.9%, $p = 0.88$). CONCLUSIONS: The IP(DVP) is influenced by pressure wave reflection. The effects of albuterol on IP(DVP) are mediated in part through the nitric oxide pathway and are impaired in patients with type II diabetes.
SO Journal of the American College of Cardiology, (**1999**) 34/7 (2007-2014).
Refs: 31
ISSN: 0735-1097 CODEN: JACCDI
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CT Medical Descriptors:
*pulse wave
*photoelectric plethysmography
*non insulin dependent diabetes mellitus
*vasodilatation
*beta adrenergic stimulation
blood vessel function
aorta bifurcation
forearm blood flow
drug effect
arterial pressure
blood flow velocity
human
male
female
clinical article
controlled study
adult
intraarterial drug administration
article
priority journal
*salbutamol
*glyceryl trinitrate
*n(g) methylarginine
*nitric oxide

L15 ANSWER 23 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999280299 EMBASE
TITLE: Evaluation of different approaches for prevention of intrauterine adhesions following hysteroscopic metroplasty for septate uterus.

AUTHOR: Shawki O.A.; Ebrashi A.N.; Kandeel H.O.; Soliman E.M.; Saleet M.E.
CORPORATE SOURCE: Dr. A.N. Ebrashi, No 2 Shafik St., Maadi, Cairo, Egypt. ebrashy3@yahoo.com
SOURCE: Middle East Fertility Society Journal, (1999) 4/2 (135-139).
Refs: 23
ISSN: 1110-5690 CODEN: MEFJFF
COUNTRY: Egypt
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Objective: To evaluate the best method for the prevention of intrauterine adhesions (IUA) following metroplasty for a septate uterus. Design: Prospective study. Settings: Department of Obstetrics and Gynecology, Kaser El Aini Hospital, Cairo university. Patients: Fifteen cases were enrolled in the study, all had recurrent first trimester pregnancy loss. Patient age ranged between 24 and 32 years. Intervention: All patients were subjected to hysteroscopic removal of the septum during the follicular phase of the cycle without prior preparation for the endometrium. Postoperatively, the patients were managed as follows: five patients did not use any postoperative prophylaxis, five cases received conjugated estrogen and progestogen for three successive cycles, and five cases had an intrauterine contraceptive device (IUD) inserted immediately postoperatively for one cycle. Second look hysteroscopy was performed after three cycles to assess the uterine cavity, the extent of adhesions and lysis of adhesions was carried out if required. Results: Postoperative intrauterine adhesions (IUA) were found in 3 patients: one in the group allocated to use conjugated estrogen, second one was in the group with IUD being inserted postoperatively. The last patient was in the control group who was not allocated to use any postoperative treatment. The adhesions found in the three patients were filmy adhesions mainly at the fundus. A residual fundal **notch**, less than 1 cm, was found in 7 cases for which no treatment was required. Conclusion: Insertion of IUD seems to be unnecessary for a favorable morphological outcome since IUA found in all cases were filmy fundal adhesions at the base of the treated area. Moreover, we found that the IUD insertion seemed to increase the likelihood of infection as well as uterine bleeding and abdominal cramps. The use of postoperative estrogen to reepithelize the freshly dissected surfaces may be harmless but seems to be optional and carries no additional benefits in prevention of IUA.
SO Middle East Fertility Society Journal, (1999) 4/2 (135-139).
Refs: 23
ISSN: 1110-5690 CODEN: MEFJFF
AB . . . any postoperative treatment. The adhesions found in the three patients were filmy adhesions mainly at the fundus. A residual fundal **notch**, less than 1 cm, was found in 7 cases for which no treatment was required. Conclusion: Insertion of IUD seems. . .
CT Medical Descriptors:
*uterus . . . CO, complication
postoperative complication: PC, prevention
postoperative infection: CO, complication
postoperative infection: DT, drug therapy
postoperative infection: PC, prevention
antibiotic prophylaxis
intrauterine contraceptive device
estrogen therapy
human
female
clinical article
controlled study
adult
oral drug administration
intravenous drug administration
article
antibiotic agent: AD, drug administration
antibiotic agent: DT, drug therapy
sultamicillin: AD, drug administration
sultamicillin: DT, drug therapy
estrogen: AD, drug administration
estrogen: DO, drug dose
prempak: AD, drug administration
prempak: DO, drug dose

L15 ANSWER 24 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999181695 EMBASE
TITLE: The effect of cryotherapy on intraarticular temperature and postoperative care after anterior cruciate ligament reconstruction.
AUTHOR: Ohkoshi Y.; Ohkoshi M.; Nagasaki S.; Ono A.; Hashimoto T.; Yamane S.
CORPORATE SOURCE: Dr. Y. Ohkoshi, Department of Orthopaedic Surgery, Hakodate Central General Hospital, 33-2 Hon-cho, Hakodate 040, Japan
SOURCE: American Journal of Sports Medicine, (1999) 27/3 (357-362).
Refs: 21
ISSN: 0363-5465 CODEN: AJSMDO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The objective of this study was to elucidate how cryotherapy after anterior cruciate ligament reconstruction affects intraarticular temperature and clinical results. A prospective and randomized study was performed on 21 knees of 21 patients. The ligament reconstruction was performed by single- incision arthroscopy using autogenous hamstring tendon. On completion of the surgery, thermosensors were implanted in the suprapatellar pouch and the intracondylar **notch**, and the intraarticular temperature was monitored while the joint was cooled. Cooling was performed in one group at 5.degree.C (N = 7) and in another at 10.degree.C (N = 7), for 48 hours. A control group (N = 7) did not undergo cryotherapy. The cooled groups showed three temperature phases: a low-temperature phase immediately after the ligament reconstruction, followed by a temperature-rising phase and a thermostatic phase. The control group had no low-temperature phase and immediately entered a thermostatic phase. During the low-temperature phase in the treated groups, the temperature of the suprapatellar pouch and of the

intercondylar **notch** were significantly lower than the body temperature. The pain score and the number of times an analgesic had to be **administered** were both significantly lower in the 10.degree.C group than in the control group. Blood loss was significantly less in the 5.degree.C group than in the control group.

SO American Journal of Sports Medicine, (**1999**) 27/3 (357-362).
Refs: 21
ISSN: 0363-5465 CODEN: AJSMDO

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L15 ANSWER 25 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999180971 EMBASE
TITLE: [Peribulbar anesthesia for peroperative and postoperative pain control in eye enucleation or evisceration: 31 cases]. L'ANESTHESIE PERIBULBAIRE POUR LE CONTROLE DE LA DOULEUR PER ET POSTOPERATOIRE AU COURS DES ENUCLEATIONS OU EVISCERATIONS. TRENTE ET UN CAS.
AUTHOR: Calenda E.; Retout A.; Muraine M.
CORPORATE SOURCE: E. Calenda, Departement d'Anesthesie Reanimation, Centre Hospitalier Univ. de Rouen, 1, rue de Germont, 76031 Rouen Cedex, France
SOURCE: Journal Francais d'Ophtalmologie, (**1999**) 22/4 (426-430).
Refs: 11
ISSN: 0181-5512 CODEN: JFOPDG
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
024 Anesthesiology
037 Drug Literature Index
LANGUAGE: French
SUMMARY LANGUAGE: English; French

AB Objectives: The aim of this prospective study was to assess peroperative and postoperative analgesia in eye enucleation or evisceration performed under peribulbar anesthesia. Patients and methods: We report 31 patients undergoing an eye enucleation (17 cases) or evisceration (14 cases). The surgical procedure was performed under local anesthesia alone in 22 patients. General anesthesia was associated with local anesthesia in 9 patients. Peribulbar block was achieved with the first insertion of the needle parallel to the inferior orbital floor and the second at level of supraorbital **notch**. A mixed anesthetic solution of equal quantity of lidocaine 2% with epinephrine (0.25 mg/20 ml) and bupivacaine 0.50% with epinephrine (0.10 mg/20 ml) was injected (total quantity 16.8 +/- 4.3 ml). Results : To assess the peroperative pain we considered the patients with local anesthesia only (22 patients). One of these 22 patients needed one injection (0.50 mg/kg) of propofol for cutting the optic nerve. Surgery was ended without any other drug but that case was considered as a failure. Peroperative analgesia was obtained in 21 of 22 patients (95.4%). To assess analgesia in the postoperative period we included 31 patients: Analgesia was complete from the accomplishment of the peribulbar block to the 4th hour in all patients (efficacy 100%). From the 4th to the 24th hour, pain remained absent in 11 (enucleation 10 cases and evisceration 1 case) of the 31 patients and no drug was used. In 20 patients (enucleation 7 cases and evisceration 13 cases), pain appeared between the 4th and the loth hour and patients were relieved by paracetamol alone in 14 cases (enucleation 6 cases and evisceration 8 cases) or by its association with nalbuphine in 5 cases (enucleation 1 case and evisceration 4 cases). In one patient (evisceration) the association of the drugs was uneffective. Conclusion: Peribulbar anesthesia is safe and generates major postoperative analgesia so we suggest to offer that technique to patients undergoing evisceration or enucleation.

SO Journal Francais d'Ophtalmologie, (**1999**) 22/4 (426-430).
Refs: 11
ISSN: 0181-5512 CODEN: JFOPDG

AB . . . with the first insertion of the needle parallel to the inferior orbital floor and the second at level of supraorbital **notch**. A mixed anesthetic solution of equal quantity of lidocaine 2% with epinephrine (0.25 mg/20 ml) and bupivacaine 0.50% with epinephrine. . .

CT Medical Descriptors:
*peribulbar anesthesia
*enucleation
*evisceration
postoperative pain
pain assessment
surgical approach
local anesthesia
analgesia
postoperative period
intraoperative period
safety
technique
human
clinical article
article
***anesthetic agent: AD, drug administration**
lidocaine: AD, drug administration
adrenalin: AD, drug administration
bupivacaine: AD, drug administration
propofol: AD, drug administration
flunitrazepam
midazolam
paracetamol
nalbuphine

L15 ANSWER 26 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999152075 EMBASE
TITLE: The effect of isosorbide dinitrate on placental blood flow and maternal blood pressure in women with pregnancy induced hypertension.
AUTHOR: Thaler I.; Amit A.; Kamil D.; Itskovitz-Eldor J.
CORPORATE SOURCE: Dr. J. Itskovitz-Eldor, Department of Obstetrics/Gynecology, Rambam Medical Center, 2 Haaliah

Street, Haifa 31096, Israel
SOURCE: American Journal of Hypertension, (1999) 12/4 I (341-347).
Refs: 30
ISSN: 0895-7061 CODEN: AJHYE6
PUBLISHER IDENT.: S 0895-7061(98)00249-0
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The effect of isosorbide dinitrate (ISDN) on maternal and fetal circulation was assessed in 23 women with pregnancy induced hypertension (PIH). A double-blind randomized design was employed. Each woman was given a sublingual tablet of ISDN (5 mg) or placebo. Maternal blood pressure (BP) and heart rate (HR) were measured before and every 2 min after the medication or placebo, for a total of 20 min. Flow velocity waveforms in the uterine and umbilical arteries were recorded at the same time periods, using pulsed Doppler ultrasound. The ratio of peak systolic to end-diastolic flow velocity (S/D) in those vessels was calculated. After ISDN mean maternal BP fell from 103 .+-. 1.8 mm Hg to 90.5 .+-. 2.9 mm Hg at 14 min (P < .0001) and mean maternal HR increased from 97.3 .+-. 3.8 beats/min to 115.7 .+-. 3.5 beats/min at 12 min (P < .0001). The mean S/D in the umbilical artery fell from 3.07 .+-. 0.33 to 2.58 .+-. 0.23 at 8 min (P < .0007). The mean S/D in the uterine artery fell from 3.27 .+-. 0.6 to 2.38 .+-. 0.28 at 10 min (P < .0001). In seven of 12 women with an early diastolic **notch** in the uterine artery flow velocity waveform the **notch** diminished or disappeared within the first 6 min after the medication. No significant change in any of the measured parameters was observed in the placebo group. Our finding that ISDN altered maternal and fetal hemodynamics in PIH lends support to the further exploration of nitric oxide donors in the treatment and prevention of pregnancy induced hypertension.
SO American Journal of Hypertension, (1999) 12/4 I (341-347).
Refs: 30
ISSN: 0895-7061 CODEN: AJHYE6
AB . . . 0.6 to 2.38 .+-. 0.28 at 10 min (P < .0001). In seven of 12 women with an early diastolic **notch** in the uterine artery flow velocity waveform the **notch** diminished or disappeared within the first 6 min after the medication. No significant change in any of the measured parameters. . .
CT Medical Descriptors:
*placenta circulation
*maternal blood
*maternal hypertension: DT, drug therapy
blood pressure
heart rate
flow rate
doppler flowmetry
hemodynamics
uterine artery
umbilical artery
drug effect
human
female
clinical article
clinical trial
randomized controlled trial
double blind procedure
controlled study
adult
sublingual drug administration
article
priority journal
*isosorbide dinitrate: CT, clinical trial
*isosorbide dinitrate: DT, drug therapy
*isosorbide dinitrate: PD, pharmacology
nitric oxide donor: CT, clinical trial
nitric. . .

L15 ANSWER 27 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999060523 EMBASE
TITLE: Early repolarization.
AUTHOR: Mehta M.; Jain A.C.; Mehta A.
CORPORATE SOURCE: Dr. M. Mehta, West Virginia University, Section of Cardiology, 2203 R. C. B. Hlth. Sci. Ctr. South, P.O. Box 9157, Morgantown, WV 26506-9157, United States
SOURCE: Clinical Cardiology, (1999) 22/2 (59-65).
Refs: 82
ISSN: 0160-9289 CODEN: CLCADC
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Early repolarization (ER) is an enigma. The purpose of this review is to reemphasize the overall electrocardiographic (ECG) pattern of this normal ST variant which continues to challenge the clinician because of its similarity to the current of injury potential to myocardium or an acute pericarditis. The data were provided from the studies identified through computerized searches of Medline, Toxline, Oxford, Agricola, and Bios Afterdark, Cumulative index, and a review of bibliographies of relevant articles on the related subjects. Early repolarization has elevated, upward, concave ST segments, located commonly in precordial leads, with reciprocal depression in aVR, tall, peaked and slightly asymmetrical T waves with **notch**, and slur on the R wave. The other accompanying features in the ECG are vertical axis, shorter and depressed P-R interval, abrupt transition, counterclockwise rotation, presence of U waves, and sinus bradycardia. Males dominate and patients are often younger than 50 years of age. The incidence of 1 to 2% is found equally common in all races. Degree and incidence of ST elevation decrease as age advances. Exercise or isoproterenol **administration** may normalize the ST segment. Early repolarization is a benign condition. If the ECG conforms to a classical pattern of ER on serial ECGs, it would exclude the unnecessary hazards of present day revascularization therapy for myocardial infarction such as primary angioplasty or thrombolytic therapy, or aggressive management of acute pericarditis, and so forth. This review concludes with a discussion of comparative ECG features of ER, pericarditis, and myocardial infarction, and provides an algorithm for

diagnostic management of patients suffering from these conditions.
SO Clinical Cardiology, (1999) 22/2 (59-65).
Refs: 82
ISSN: 0160-9289 CODEN: CLCADC
AB . . . ST segments, located commonly in precordial leads, with reciprocal depression in aVR, tall, peaked and slightly asymmetrical T waves with **notch**, and slur on the R wave. The other accompanying features in the ECG are vertical axis, shorter and depressed P-R. . . is found equally common in all races. Degree and incidence of ST elevation decrease as age advances. Exercise or isoproterenol **administration** may normalize the ST segment. Early repolarization is a benign condition. If the ECG conforms to a classical pattern of. . .

L15 ANSWER 28 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998326470 EMBASE
TITLE: Peripheral neuropathy in transgenic diabetic mice: Restoration of C- fiber function with human recombinant nerve growth factor.
AUTHOR: Elias K.A.; Cronin M.J.; Stewart T.A.; Carlsen R.C.
CORPORATE SOURCE: Dr. K.A. Elias, Genentech, Inc., 1 DNA Way, South, San Francisco, CA 94080, United States. kelias@gene.com
SOURCE: Diabetes, (1998) 47/10 (1637-1642).
Refs: 35
ISSN: 0012-1797 CODEN: DIAEAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
008 Neurology and Neurosurgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Mice (Ins.D(d)1) with hypoinsulinemic diabetes were created by increased expression of syngeneic major histocompatibility complex (MHC) class I protein in pancreatic .beta.-cells. The diabetic state was characterized in these mice by high glucose concentrations and islet pathology. To determine whether a neuropathy would develop, motor and sensory conduction velocities (CV) were determined in the sciatic nerves of 2-, 4-, and 7-month-old control and diabetic littermate male mice. Recording bipolar electrodes were placed in the plantar muscles of the hind foot of anesthetized (ketamine/xylazine) mice. Bipolar stimulating electrodes were positioned near the sciatic nerve at the sciatic **notch** or near the tibial nerve at the ankle. Motor CV from .alpha.- motor fibers and sensory CV from proprioceptive A.alpha. nerves were measured and expressed as meters per second (m/s). Group data are reported as mean .+-. SE and compared by analysis of variance. The CVs from nondiabetic mice (controls) were not different across the three ages and averaged 41.3 .+-. 1.7 m/s for motor and 38.7 .+-. 1.7 m/s for sensory. The motor CVs from diabetic mice at 2 and 4 months were similar to controls. Sensory CVs were unchanged at 2 months but were lower at 4 months (18.9 .+-. 2.4 m/s). Both sensory (23.9 .+-. 2.1 m/s) and motor (18.9 .+-. 1.8 m/s) CVs were significantly reduced at 7 months, which is indicative of a polyneuropathy. NGF has well-known trophic effects on sympathetic and small sensory neurons. To determine whether NGF could influence this neuropathy, 6-month-old control and diabetic mice were divided into the following groups: 1) control + vehicle, 2) diabetic + vehicle, and 3) diabetic + NGF (1 mg/kg, 3 x week, s.c.). After 1 month of treatment, motor and sensory CVs were determined. In some mice, the branches of the sciatic nerve were exposed and in situ recordings from the sural nerve were performed to determine compound C-fiber CV, integral, and amplitude. Sensory CV, determined via Hoffmann's reflex (H-reflex) (A-fiber), was decreased in diabetic compared with control animals as expected ($P < 0.05$), and NGF did not alter this parameter. Continuing diabetes reduced the amplitude (0.9 .+-. 0.2 vs. 3.2 .+-. 0.7 mV x 10-2; $P < 0.05$) and integral (6.9 .+-. 1.9 mV/ms vs. 18.8 .+-. 4.4 mV/ms; $P < 0.05$) of the C-fiber response versus control, suggesting fiber loss. NGF treatment normalized C-fiber amplitude (2.9 .+-. 0.8 mV x 10-2) and integral (21.2 .+-. 6.5 mV/ms) in animals with established diabetes, with no effect on blood glucose. The C-fiber CV was similar in all groups, indicating that the animals had some normally conducting small fiber sensory nerves. These studies characterized a motor and sensory polyneuropathy in transgenic diabetic mice and are the first to demonstrate directly that NGF treatment can protect or restore abnormal sensory C-fiber function.
SO Diabetes, (1998) 47/10 (1637-1642).
Refs: 35
ISSN: 0012-1797 CODEN: DIAEAZ
AB . . . of the hind foot of anesthetized (ketamine/xylazine) mice. Bipolar stimulating electrodes were positioned near the sciatic nerve at the sciatic **notch** or near the tibial nerve at the ankle. Motor CV from .alpha.- motor fibers and sensory CV from proprioceptive A.alpha.. . .
CT Medical Descriptors:
*diabetes mellitus
*peripheral neuropathy: CO, complication
transgenic mouse
sciatic nerve
tibial nerve
sural nerve
nerve fiber c
nerve conduction
nonhuman
mouse
animal model
controlled study
subcutaneous drug administration
article
priority journal
*recombinant nerve growth factor

L15 ANSWER 29 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998302178 EMBASE
TITLE: Minimal-access aortic and valvular operations, including the 'J/j' incision.
AUTHOR: Svensson L.G.; D'Agostino R.S.
CORPORATE SOURCE: Dr. L.G. Svensson, Department of Thoracic Surgery, Lahey Hitchcock Clinic, 41 Mall Rd, Burlington, MA 01805, United States
SOURCE: Annals of Thoracic Surgery, (1998) 66/2 (431-435).
Refs: 8
ISSN: 0003-4975 CODEN: ATHSAK
PUBLISHER IDENT.: S 0003-4975(98)00462-7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 009 Surgery
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background. We compared five current minimal-access approaches, namely, parasternal incision, transverse sternotomy, manubrial inverted 'T' incision, incomplete mediastinotomy, and our 'J/j' incision, to operations in matched patients, including aortic operations. Methods. In a case-control study of 74 patients, 37 individuals consecutively underwent minimal-access operations (aortic valve, 18, including one mitral valve operation; composite valve graft, six, including one arch and one transaortic mitral valve operation for a patient with Marfan's syndrome; ascending aorta operation, two; root repair/reconstruction, three; mitral valve repair/replacement, seven, including one maze operation; and atrioseptal defect repair, one). The patients were matched by sex, age, surgeon, and operation with 37 control patients who had standard incisions. Patients having the 'J/j' incision (n = 25) had sternotomies from the first right intercostal space, or sternal **notch**, to the third to fifth right intercostal space. Results. Minimal- access patients had a shorter postoperative hospital stay than standard incision patients (6.2 versus 8.2 days; p = 0.0055), and required similar volumes of blood (0.86 versus 1.03 units; p = 0.7243), postoperative morphine dosages (28 mg versus 40 mg, p = 0.0643), and oral narcotics (8.1 versus 10.0 doses; p = 0.3562). 'J/j' incision patients, however, required less morphine (20.6 mg versus 40.9 mg; p = 0.0028), but not fewer doses of oral narcotics (7.5 versus 9.9 doses; p = 0.2640) and had the shortest postoperative stay (5.1 versus 8.1 days; p < 0.0001). No stroke or clinically noted neurocognitive deficit developed. One minimal-access patient (1/37, 2.7%) with severe preoperative pulmonary morbidity died of adult respiratory distress syndrome. Sternal nonunion developed in 1 patient with an inverted 'T' manubrial incision. In a further seven patients, the 'J/j' incision was used without a problem, for a total of 32 patients. This compared with a consecutive series of 125 aortic valve replacement operations without a death and 181 patients undergoing ascending arch operations with two 30-day hospital deaths (1.1%) and two strokes (1.1%). Conclusion. Minimal-access incisions are associated with shorter hospital stays. For the 'J/j' incision, even if used for more extensive double-valve, ascending aortic arch, or composite valve operations, postoperative pain appears to be less and patients are discharged even earlier.

SO Annals of Thoracic Surgery, (1998) 66/2 (431-435).
Refs: 8
ISSN: 0003-4975 CODEN: ATHSAK

AB . . . standard incisions. Patients having the 'J/j' incision (n = 25) had sternotomies from the first right intercostal space, or sternal **notch**, to the third to fifth right intercostal space. Results. Minimal- access patients had a shorter postoperative hospital stay than standard. . .

CT Medical Descriptors:
*aorta . . . defect: SU, surgery
length of stay
sternotomy
surgical technique
ascending aorta
aorta arch
postoperative pain: CO, complication
postoperative pain: DT, drug therapy
postoperative pain: PC, prevention
work resumption
human
male
female
clinical article
controlled study
aged
adult
oral drug administration
intravenous drug administration
article
priority journal
***narcotic analgesic agent: AD, drug administration**
*narcotic analgesic agent: DO, drug dose
*narcotic analgesic agent: DT, drug therapy
morphine: AD, drug administration
morphine: DO, drug dose
morphine: DT, drug therapy

L15 ANSWER 30 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998271581 EMBASE
TITLE: Use of a lighted stylet for intubation via the laryngeal mask airway.
AUTHOR: Agro F.; Brimacombe J.; Carassiti M.; Morelli A.; Giampalmo M.; Cataldo R.
CORPORATE SOURCE: Dr. J. Brimacombe, Dept. of Anaesthesia/Intensive Care, University of Queensland, Cairns Base Hospital, Cairns, QLD 4870, Australia. 100236,2343@compuserve.com
SOURCE: Canadian Journal of Anaesthesia, (1998) 45/6 (556-560).
Refs: 21
ISSN: 0832-610X CODEN: CJOAEP
COUNTRY: Canada
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 009 Surgery
024 Anesthesiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English; French

AB Purpose: To assess a new technique for intubation via the laryngeal mask airway (LMA) in which a lighted stylet is used to optimise the position of the LMA before intubation. Methods: In 114 patients, following LMA insertion, the lighted stylet (Trachlight Wand.RTM.) with mounted tracheal tube (TT) was advanced 1.5 cm beyond the mask aperture bars and the anterior neck observed for a distinct central point of light at the cricothyroid membrane (CTM). If this was not seen, the LMA was repositioned in the pharynx, depending on the location of the light, by manually advancing, withdrawing or rotating the device, manipulating the head/neck or trying an alternative size. Tracheal intubation was attempted only when transillumination was correct. The TT with lighted stylet was advanced until the supra-sternal **notch** was transilluminated.
Results: In 89 patients (78%) the CTM was transilluminated without repositioning in 12 (10%) a single positional adjustment was required, and in 10 (9%) a change of LMA size was required. In three patients (3%) transillumination of the CTM was impossible. In the 97% of patients in

whom transillumination was correct, tracheal intubation was successful in all at the first attempt without the need for further repositioning or size change. Conclusion: The lighted stylet is useful in facilitating intubation via the LMA in anaesthetised adult patients when used as a guide to optimal LMA position.

SO Canadian Journal of Anaesthesia, (1998) 45/6 (556-560).
Refs: 21
ISSN: 0832-610X CODEN: CJOAEP

AB . . . size. Tracheal intubation was attempted only when transillumination was correct. The TT with lighted stylet was advanced until the supra-sternal **notch** was transilluminated. Results: In 89 patients (78%) the CTM was transilluminated without repositioning in 12 (10%) a single positional adjustment. . .

CT Medical Descriptors:
*laryngeal mask
*endotracheal intubation
anesthetic equipment
technique
endotracheal tube
position
elective surgery
human
male
female
major clinical study
aged
adult
intravenous drug administration
article
priority journal
midazolam
propofol
fentanyl

L15 ANSWER 31 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998186553 EMBASE
TITLE: Estrogen replacement, vascular distensibility, and blood pressures in postmenopausal women.
AUTHOR: De Meersman R.E.; Zion A.S.; Giardina E.G.V.; Weir J.P.; Lieberman J.S.; Downey J.A.
CORPORATE SOURCE: R.E. De Meersman, Columbia Univ., Box 38, 630 W. 168th St., New York, NY 10032, United States
SOURCE: American Journal of Physiology - Heart and Circulatory Physiology, (1998) 274/5 43-5 (H1539-H1544).
Refs: 34
ISSN: 0363-6135 CODEN: AJPPDI
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The pathogenesis of blood pressure (BP) rise in aging women remains unexplained, and one of the many incriminating factors may include abnormalities in arteriolar resistance vessels. The aim of this study was to determine the effects of unopposed estrogen on arteriolar distensibility, baroreceptor sensitivity (BRS), BP changes, and rate-pressure product (RPP). We tested the hypotheses that estrogen replacement therapy (ERT) enhances arteriolar distensibility and ameliorates BRS, which leads to decreases in BP and RPP. Postmenopausal women participated in a single-blind crossover study; the participants of this study, after baseline measurements, were randomly assigned to receive estrogen (ERT) or a drug-free treatment with a 6-wk washout period between treatments. The single-blind design was instituted because subjects become unblinded due to physiological changes (i.e., fluid shifts, weight gain, and secretory changes) associated with estrogen intake. However, investigators and technicians involved in data collection and analyses remained blind. After each treatment, subjects performed identical autonomic tests, during which electrocardiograms, beat-by-beat BPs, and respiration were recorded. The area under the dicrotic **notch** of the BP wave was used as an index of arteriolar distensibility. The magnitude of the reflex bradycardia after a precipitous rise in BP was used to determine BRS. Power spectral analysis of heart rate variability was used to assess autonomic activity. BPs were recorded from resistance vessels in the finger using a beat-by-beat photoplethysmographic device. RPP, a noninvasive marker of myocardial oxygen consumption, was calculated. Repeated-measures analyses of variance revealed a significantly enhanced arteriolar distensibility and BRS after ERT ($P < 0.05$). A trend of a lower sympathovagal balance at rest was observed after ERT; however, this trend did not reach statistical significance ($P = 0.061$) compared with the other treatments. The above autonomic changes produced significantly lower systolic and diastolic BP changes and RPPs ($P < 0.05$) at rest and during isometric exercise. We conclude that short-term unopposed ERT favorably enhances arteriolar distensibility, BRS, and hemodynamic parameters in postmenopausal women. These findings have clinical implications in the goals for treating cardiovascular risk factors in aging women.

SO American Journal of Physiology - Heart and Circulatory Physiology, (1998) 274/5 43-5 (H1539-H1544).
Refs: 34
ISSN: 0363-6135 CODEN: AJPPDI

AB . . . treatment, subjects performed identical autonomic tests, during which electrocardiograms, beat-by-beat BPs, and respiration were recorded. The area under the dicrotic **notch** of the BP wave was used as an index of arteriolar distensibility. The magnitude of the reflex bradycardia after a. . .

CT Medical Descriptors:
*hypertension
*postmenopause
*aging
ischemic heart disease
resistance blood vessel
estrogen therapy
risk factor
coronary risk
pressoreceptor reflex
human
female
human experiment
normal human
clinical trial
randomized controlled trial
single blind procedure

crossover procedure
controlled study
oral drug administration
article
priority journal
*conjugated estrogen: CT, clinical trial
***conjugated estrogen: AD, drug administration**
*conjugated estrogen: DO, drug dose
*conjugated estrogen: PD, pharmacology
estrogen

L15 ANSWER 32 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998065707 EMBASE
TITLE: Economic and humanitarian contribution of Wisconsin's family medicine residencies.
AUTHOR: Hueston W.J.; Baumgardner D.J.; Turkal N.W.; Eliason B.C.; Beasley J.W.
CORPORATE SOURCE: Dr. D.J. Baumgardner, St. Luke's Family Practice Residency, 2901 W. Kinnickinnic River Parkway, Milwaukee, WI 53215, United States
SOURCE: Wisconsin Medical Journal, (1998) 97/2 (38-42).
Refs: 14
ISSN: 0043-6542 CODEN: WMJOA7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
036 Health Policy, Economics and Management
LANGUAGE: English
SUMMARY LANGUAGE: English
AB BACKGROUND: Family practice residencies have historically been funded by a combination of clinical income, medicare pass-through funding and state and federal grants. In this era of cost containment, residencies are forced to increasingly rely on clinical income to remain solvent. This paper examines the fiscal and humanitarian contributions of Wisconsin's family practice residency programs that may not be reimbursed by clinical funds. METHODS: Data were elicited from Wisconsin's Family Practice Residency Programs by mail survey. RESULTS: The combined twelve family practice programs in Wisconsin have nearly 300,000 patient visits per year (mean per program surveyed 25,000 per year). Fifty-five percent of the patients are covered by Medicare and Medicaid. Uncompensated care amounts to over $1.4 million/year. In addition, many other direct and indirect services are provided. The combined residency programs have had 1,239 graduates with 715 (58%) currently practicing in Wisconsin, many in underserved areas. CONCLUSIONS: The family practice residencies in Wisconsin train many of the state's primary care physicians and provide many services to their institutions and communities, including significant clinical service to the poor and underserved. The 12 Wisconsin Family Practice Residency Programs are responding to the enhanced need for generalist physicians by increasing residency slots, attracting top-**notch** applicants, many with personal ties to the state, 2 and by increasing the diversity of training sites. These programs have already contributed substantially to the supply of generalist physicians in our state. Family Practice residencies are continuously under scrutiny by their sponsoring institutions regarding the financial burdens that they create, and a few programs close each year, primarily for perceived financial reasons. Historically, most programs have been able to demonstrate budget neutrality or even significant surpluses by (somewhat arbitrary) cost-benefit analyses. In these scenarios, the deficits remaining from shortfalls in clinical income generated by the program residents and faculty were generally offset by Medicare payments for graduate medical education reimbursement, and state and federal grants. Wisconsin Family Practice programs now face increased economic pressures due to: 1. Increased faculty and **administrative**/accounting resources required to fulfill Medicare billing guidelines for patients seen by residents. 2. Increased managed care activity in which formerly revenue- generating clinical activities are viewed as expenses. 3. The possibility of significant cuts in Medicare payments for graduate medical education. This article focuses on the impact of family practice residencies on the delivery of care and supply of famil doctors in the State of Winconsin, and their contribution to healthcare for the less affluent indigent.
SO Wisconsin Medical Journal, (1998) 97/2 (38-42).
Refs: 14
ISSN: 0043-6542 CODEN: WMJOA7
AB . . . Wisconsin Family Practice Residency Programs are responding to the enhanced need for generalist physicians by increasing residency slots, attracting top- **notch** applicants, many with personal ties to the state, 2 and by increasing the diversity of training sites. These programs have. . . and state and federal grants. Wisconsin Family Practice programs now face increased economic pressures due to: 1. Increased faculty and **administrative**/accounting resources required to fulfill Medicare billing guidelines for patients seen by residents. 2. Increased managed care activity in which formerly. . .

L15 ANSWER 33 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97176097 EMBASE
DOCUMENT NUMBER: 1997176097
TITLE: Desferrioxamine ototoxicity in an adult transfusion-dependent population.
AUTHOR: Chiodo A.A.; Alberti P.W.; Sher G.D.; Francombe W.H.; Tyler B.
CORPORATE SOURCE: Dr. P.W. Alberti, Department of Otolaryngology, Toronto Hospital, University of Toronto, 200 Elizabeth Street, Toronto, Ont. M5G 2C4, Canada
SOURCE: Journal of Otolaryngology, (1997) 26/2 (116-122).
Refs: 21
ISSN: 0381-6605 CODEN: JOTODX
COUNTRY: Canada
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 011 Otorhinolaryngology
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English; French
AB Objective: The purpose of this study was to identify the incidence of hearing loss in a population of 75 adult (19-68 years old) transfusion-dependent patients with thalassemia major, sickle cell disease, Diamond-Blackfan anemia, and various other hematologic disorders treated with regular transfusion schedules. Ninety-three percent (70/75) of patients had a history of long-term subcutaneous or intravenous desferrioxamine therapy. Methods: The patients underwent routine otolaryngologic history and physical examination, along with standard

pure-tone audiometry at 250, 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hz, with hearing loss defined as 25 dB or greater at one or more frequencies. Results: Hearing loss was present in 57% (43/75) of patients. More importantly, hearing loss attributable to desferrioxamine ototoxicity was present in 29%. (22/75) of patients. Sixteen patients treated previously with desferrioxamine were switched to the experimental oral chelating agent, L1. Eight of these 16 patients had hearing loss attributable to desferrioxamine, with 5 of these patients worsening with the experimental oral chelating agent L1. Seventy-nine percent (59/75) of patients were thalassemic. Fifty-four percent (33/59) of these thalassemic patients had hearing loss. However, 35% (21/59) of the thalassemic patients had hearing loss attributable to desferrioxamine ototoxicity. All thalassemic patients with desferrioxamine ototoxicity had high-frequency sensorineural hearing loss, with 33% (7/21) having a **notch** at 6 kHz. In addition, 5% (1/21) had notching at 3 khz. Few of the hearing losses were disabling. Conclusions: Management of these patients requires proper dosing of desferrioxamine and transfusion therapy, along with regular monitoring of body iron burden and hemoglobin. In addition, regular otolaryngologic and audiometric follow-up with special care to include the frequencies of 3 and 6 kHz may help recognize and prevent permanent ototoxicity.

SO Journal of Otolaryngology, (1997) 26/2 (116-122).
Refs: 21
ISSN: 0381-6605 CODEN: JOTODX

AB . . . attributable to desferrioxamine ototoxicity. All thalassemic patients with desferrioxamine ototoxicity had high-frequency sensorineural hearing loss, with 33% (7/21) having a **notch** at 6 kHz. In addition, 5% (1/21) had notching at 3 khz. Few of the hearing losses were disabling. Conclusions:. . .

CT Medical Descriptors:
*blood transfusion
*iron blood level
*ototoxicity: ET, etiology
*ototoxicity: DI, diagnosis
*ototoxicity: SI, side effect
*ototoxicity: CO, complication
*ototoxicity: PC, prevention
adult
aged
article
blackfan diamond anemia: TH, therapy
female
human
intravenous drug administration
major clinical study
male
priority journal
sickle cell anemia: TH, therapy
subcutaneous drug administration
thalassemia major: TH, therapy
*deferoxamine: AE, adverse drug reaction
*deferoxamine: DT, drug therapy
*iron: EC, endogenous compound
deferoxamine mesylate

L15 ANSWER 34 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97068236 EMBASE
DOCUMENT NUMBER: 1997068236
TITLE: Effect of low-dose aspirin treatment on vascular resistance in the uterine, uteroplacental, renal and umbilical arteries - A prospective longitudinal study on a high risk population with persistent **notch** in the uterine arteries.
AUTHOR: Zimmermann P.; Eirio V.; Koskinen J.; Niemi K.; Nyman R.; Kujansuu E.; Ranta T.
CORPORATE SOURCE: P. Zimmermann, Vellamontie 4, FIN-15870 Hollola, Finland
SOURCE: European Journal of Ultrasound, (1997) 5/1 (17-30).
Refs: 37
ISSN: 0929-8266 CODEN: EJULE8
PUBLISHER IDENT.: S 0929-8266(96)00203-0
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
014 Radiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Objective: The study focuses on the changes of Doppler flow velocity waveforms in the uterine, uteroplacental, maternal intrarenal and umbilical artery in a selected population at high risk for pre-eclampsia or IUGR with original abnormal Doppler of the uterine arteries, defined as persistent bilateral **notches** at 22-24 weeks of gestation, who were randomised treated with low-dose aspirin compared to no treatment and low risk controls, longitudinally during pregnancy and 6 months postpartum. Methods: High risk and control patients were collected from a population attending routine ultrasound for confirmation of gestational age. One-hundred-and-seventy-eight high risk patients and 29 normal controls had duplex pulsed wave Doppler ultrasound at 22-24 weeks of gestation, Twenty-eight high risk patients showed bilateral **notches** in the main uterine arteries. Of those 26 were randomised treated with 50 mg aspirin or had no treatment. Additional Doppler ultrasound examinations were performed twice during pregnancy at 28-32 and 33-40 weeks and once 6 months postpartum. Main outcome criteria were incidence of pregnancy induced hypertension (PIH) and intrauterine growth retardation (IUGR). Results: The **notches** in the uterine arteries in the high risk group were constant throughout pregnancy in both the aspirin and untreated group in 88.5% (23/26) of the cases, The majority of resistance indices (RI) in the main uterine and uteroplacental arteries of the high risk population ranged above the mean line registered in low risk pregnancies, whereas no differences could be seen in the renal and umbilical artery. Aspirin had no effect on the Doppler waveform in any of the examined vessels except the uteroplacental arteries. At 22-24 weeks of gestation the highest RI were found in high risk patients who developed PIH or IUGR later during pregnancy compared to high risk patients without-disease or normal controls. Six months postpartum no differences in vascular resistance were seen any more between the different groups and the RI was still lower than reported for non-pregnant women. Aspirin treatment could not prevent PIH or IUGR, but was safe for the foetus. However, in the aspirin group there was one uterine haemorrhage at 36 weeks of gestation and one placental abruption at emergency caesarean section for threatening asphyxia at 38 weeks. Persistent bilateral **notches** in high risk patients selected a group with 35% incidence

of PIH and 12% incidence of IUGR. Conclusions: Low-dose aspirin treatment does not affect the resistance index in the uterine, umbilical or renal circulation. Significant **notches** in the uterine arteries at 22-24 weeks gestation persist usually throughout pregnancy. The phenomenon is related to higher resistance indices but does not prevent 'physiological' adaptation of vascular resistance in the uterine artery during pregnancy or postpartum. Combining high risk selection and uterine Doppler at 22-24 weeks of gestation may be useful to find a group with high incidences of PIH or IUGR. However, starting low-dose aspirin treatment based on the pathological Doppler, is possibly too late for prevention of the disease.

TI . . . in the uterine, uteroplacental, renal and umbilical arteries - A prospective longitudinal study on a high risk population with persistent **notch** in the uterine arteries.

SO European Journal of Ultrasound, (**1997**) 5/1 (17-30).
Refs: 37
ISSN: 0929-8266 CODEN: EJULE8

AB . . . population at high risk for pre-eclampsia or IUGR with original abnormal Doppler of the uterine arteries, defined as persistent bilateral **notches** at 22-24 weeks of gestation, who were randomised treated with low-dose aspirin compared to no treatment and low risk controls,. . . 29 normal controls had duplex pulsed wave Doppler ultrasound at 22-24 weeks of gestation, Twenty-eight high risk patients showed bilateral **notches** in the main uterine arteries. Of those 26 were randomised treated with 50 mg aspirin or had no treatment. Additional. . . 6 months postpartum. Main outcome criteria were incidence of pregnancy induced hypertension (PIH) and intrauterine growth retardation (IUGR). Results: The **notches** in the uterine arteries in the high risk group were constant throughout pregnancy in both the aspirin and untreated group. . . 36 weeks of gestation and one placental abruption at emergency caesarean section for threatening asphyxia at 38 weeks. Persistent bilateral **notches** in high risk patients selected a group with 35% incidence of PIH and 12% incidence of IUGR. Conclusions: Low-dose aspirin treatment does not affect the resistance index in the uterine, umbilical or renal circulation. Significant **notches** in the uterine arteries at 22-24 weeks gestation persist usually throughout pregnancy. The phenomenon is related to higher resistance indices. . .

CT Medical Descriptors:
*doppler flowmetry
*high risk pregnancy: DI, diagnosis
*vascular resistance
article
clinical article
clinical trial
controlled study
female
fetus
human
kidney artery
oral drug administration
priority journal
randomized controlled trial
umbilical artery
uterine artery
*acetylsalicylic acid: DO, drug dose
*acetylsalicylic acid: CT, clinical trial
disperin
unclassified drug

L15 ANSWER 35 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96339174 EMBASE
DOCUMENT NUMBER: 1996339174
TITLE: Efficacy of antibiotics alone for orthopaedic device related infections.
AUTHOR: Isiklar Z.U.; Darouiche R.O.; Landon G.C.; Beck T.
CORPORATE SOURCE: Infectious Disease Section, Veterans Affairs Medical Center, 2002 Holcombe Boulevard,Houston, TX 77030, United States
SOURCE: Clinical Orthopaedics and Related Research, (**1996**) -/332 (184-189).
ISSN: 0009-921X CODEN: CORTBR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Treatment of orthopaedic device related infections with antibiotics alone generally has been thought to be inadequate. A rabbit model was used to compare the efficacy of 4 different antibiotic regimens for treating orthopaedic device related infection caused by slime producing Staphylococcus epidermidis. After bacterial inoculation of a hole drilled through the intercondylar **notch**, a stainless steel screw was placed into the femur. Two weeks later, rabbits were randomized to receive a 2-week course of antibiotics: (1) 9 rabbits received vancomycin alone; (2) 10 rabbits received minocycline alone; (3) 10 rabbits received vancomycin plus rifampin; and (4) 10 rabbits received minocycline plus rifampin. Quantitative bone cultures were performed, and antibiotic levels in serum, bone, and biofilm were determined. Despite high levels of vancomycin in biofilm, infection was never cured by vancomycin alone and was eradicated in only 20% of rabbits that received minocycline alone. The highest cure rate (90%) was achieved with the combination of vancomycin and rifampin, whereas the combination of minocycline and rifampin yielded a cure rate of 70%. These results encourage the clinical evaluation of the combination of vancomycin and rifampin in patients in whom infected orthopaedic device cannot be removed.

SO Clinical Orthopaedics and Related Research, (**1996**) -/332 (184-189).
ISSN: 0009-921X CODEN: CORTBR

AB . . . orthopaedic device related infection caused by slime producing Staphylococcus epidermidis. After bacterial inoculation of a hole drilled through the intercondylar **notch**, a stainless steel screw was placed into the femur. Two weeks later, rabbits were randomized to receive a 2-week course. . .

CT Medical Descriptors:
*bone screw
*postoperative infection: ET, etiology
*postoperative infection: DT, drug therapy
*staphylococcus epidermidis
animal experiment
animal model
animal tissue
article

controlled study
device
dose response
drug blood level
drug efficacy
drug mixture
drug tissue level
female
femur
intramuscular drug administration
nonhuman
oral drug administration
priority journal
rabbit
***antibiotic agent: AD, drug administration**
*antibiotic agent: CB, drug combination
*antibiotic agent: CM, drug comparison
*antibiotic agent: CR, drug concentration
*antibiotic agent: DO, drug dose
*antibiotic. . . therapy
*antibiotic agent: PD, pharmacology
*minocycline: PD, pharmacology
*minocycline: DT, drug therapy
*minocycline: DO, drug dose
*minocycline: CR, drug concentration
*minocycline: CM, drug comparison
*minocycline: CB, drug combination
***minocycline: AD, drug administration**
*rifampicin: CB, drug combination
***rifampicin: AD, drug administration**
*rifampicin: PD, pharmacology
*rifampicin: DT, drug therapy
*rifampicin: DO, drug dose
*rifampicin: CR, drug concentration
*rifampicin: CM, drug comparison
*vancomycin: PD, pharmacology
***vancomycin: AD, drug administration**
*vancomycin: CB, drug combination
*vancomycin: CM, drug comparison
*vancomycin: CR, drug concentration
*vancomycin: DO, drug dose
*vancomycin: DT, drug therapy
tetracycline

L15 ANSWER 36 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96262448 EMBASE
DOCUMENT NUMBER: 1996262448
TITLE: Supra-orbital neuralgia and its treatment.
AUTHOR: Bastiaensen L.A.K.
CORPORATE SOURCE: Nieuwe Bosscheweg 17,5017 JJ Tilburg, Netherlands
SOURCE: Neuro-Ophthalmology, (1996) 16/4 (225-227).
ISSN: 0165-8107 CODEN: NRPHDN
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
012 Ophthalmology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Supra-orbital neuralgia is a form of localized headache in or above the eyebrow with possible extension in the entire skin region of n.V-I. Its course is intermittent or chronic, its start is in the fourth or fifth decade and it is predominantly present in females. The most important hallmark is the same pain experienced by pressure on the supra-orbital **notch**. The proposed treatment is an injection of 2 ml of 2% lidocaine - 1:60,000 adrenalin in the supra-orbital channel, which relieves and mostly obviates the pain in .+-. 80% of the patients over a considerable time span.
SO Neuro-Ophthalmology, (1996) 16/4 (225-227).
ISSN: 0165-8107 CODEN: NRPHDN
AB . . . it is predominantly present in females. The most important hallmark is the same pain experienced by pressure on the supra-orbital **notch**. The proposed treatment is an injection of 2 ml of 2% lidocaine - 1:60,000 adrenalin in the supra-orbital channel, which. . .
CT Medical Descriptors:
*neuralgia: DT, drug therapy
adult
article
clinical article
female
human
male
*adrenalin: DT, drug therapy
*adrenalin: CB, drug combination
***adrenalin: AD, drug administration**
*lidocaine: DT, drug therapy
*lidocaine: CB, drug combination
***lidocaine: AD, drug administration**

L15 ANSWER 37 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96259468 EMBASE
DOCUMENT NUMBER: 1996259468
TITLE: Effects of carvedilol and atenolol on arterial pulse curves (plethysmography) and finger temperature after hand cooling.
AUTHOR: Klemsdal T.O.; Mundal H.H.; Gjesdal K.
CORPORATE SOURCE: Department of Cardiology, Ulleval University Hospital,N-0407 Oslo, Norway
SOURCE: European Journal of Clinical Pharmacology, (1996) 50/6 (483-489).
ISSN: 0031-6970 CODEN: EJCPAS
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objective: In a double-blind, parallel study, the effects of 25 mg carvedilol and 50 mg atenolol on peripheral finger circulation and arterial pulse curve configuration were compared. Methods: Healthy volunteers (n = 17) were examined at baseline and for 15 min after 60 s of

hand cooling in ice-water. Finger temperature and digital plethysmography were recorded each minute from the cooled and the control hands. Measurements were also made before and 2 h after drug **administration**. Results: Blood pressure declined from 120/86 to 108/74 mm Hg after atenolol (n = 9), and from 122/88 to 108/73 mm Hg after carvedilol (n = 8). In both groups, baseline linger temperature increased slightly after drug, and a more rapid rise in finger temperature was observed after cooling. There was no group difference in the drug effect on finger temperature, except in the first few minutes after cooling, when temperature recovery was greater after carvedilol. Carvedilol reduced the vasoconstrictor response to local cooling (digital plethysmography), compared both to the value before drug and after atenolol. At rest, carvedilol changed the pulse curves (control hand) towards vasodilatation and high compliance, expressed as a mean change in the relative height of the dicrotic **notch** of - 10.3% versus 0.0% after atenolol. Conclusion: Future studies should clarify whether the vasoactive profile of carvedilol may translate into reduced occurrence of cold hands and feet amongst patients treated for hypertension.

SO European Journal of Clinical Pharmacology, (**1996**) 50/6 (483-489).
ISSN: 0031-6970 CODEN: EJCPAS

AB . . . recorded each minute from the cooled and the control hands. Measurements were also made before and 2 h after drug **administration**. Results: Blood pressure declined from 120/86 to 108/74 mm Hg after atenolol (n = 9), and from 122/88 to 108/73. . . curves (control hand) towards vasodilatation and high compliance, expressed as a mean change in the relative height of the dicrotic **notch** of - 10.3% versus 0.0% after atenolol. Conclusion: Future studies should clarify whether the vasoactive profile of carvedilol may translate. . .

CT Medical Descriptors:
*blood pressure
*cold limb
*plethysmography
adult
article
asthenia: SI, side effect
double blind procedure
fatigue: SI, side effect
human
human experiment
male
normal human
oral drug administration
priority journal
skin temperature
syncope: SI, side effect
*atenolol: AE, adverse drug reaction
*atenolol: PD, pharmacology
*atenolol: CM, drug comparison
*carvedilol: AE, adverse drug. . .

L15 ANSWER 38 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96011621 EMBASE
DOCUMENT NUMBER: 1996011621
TITLE: A randomized controlled trial of aspirin in patients with abnormal uterine artery blood flow.
AUTHOR: Morris J.M.; Fay R.A.; Ellwood D.A.; Cook C.-M.; Devonald K.J.
CORPORATE SOURCE: Dept. of Obstetrics and Gynaecology, Maternity Department, John Radcliffe Hospital,Oxford OX3 9DU, United Kingdom
SOURCE: Obstetrics and Gynecology, (**1996**) 87/1 (74-78).
ISSN: 0029-7844 CODEN: OBGNAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Objective: To evaluate color Doppler imaging of the uterine arteries as a screening test in nulliparous women, and to examine the role of low-dose aspirin therapy in pregnancies with abnormal uteroplacental resistance. Methods: At the routine 18-week fetal morphology ultrasound scan, 955 nulliparous women underwent color Doppler imaging of the uterine arteries. Abnormal uteroplacental vascular resistance was defined with respect to both the systolic-diastolic ratio of the flow velocity waveform and the presence of an ipsilateral early diastolic **notch**. Those with abnormal uterine artery waveforms were asked to participate in a randomized controlled trial of aspirin therapy. Pregnancy outcomes were compared in women with normal or abnormal flow velocity waveforms, as well as in the two arms of the intervention study. Results: Of 186 women with abnormal uteroplacental resistance according to criteria defined previously, 102 agreed to randomization to either low-dose aspirin (100 mg/day) or placebo for the remainder of the pregnancy. Abnormal uterine artery flow velocity waveforms were associated with statistically significant increases in preeclampsia (11 versus 4%), birth weight below the tenth percentile (28 versus 11%), and adverse pregnancy outcome (45 versus 28%). Prophylactic aspirin therapy did not result in a significant reduction in pregnancy complications. Conclusion: Abnormal uteroplacental resistance at 18 weeks' gestation was associated with a significant increase in adverse pregnancy outcome. Low-dose aspirin did not reduce pregnancy complications in women with uteroplacental insufficiency.

SO Obstetrics and Gynecology, (**1996**) 87/1 (74-78).
ISSN: 0029-7844 CODEN: OBGNAS

AB . . . with respect to both the systolic-diastolic ratio of the flow velocity waveform and the presence of an ipsilateral early diastolic **notch**. Those with abnormal uterine artery waveforms were asked to participate in a randomized controlled trial of aspirin therapy. Pregnancy outcomes. . .

CT Medical Descriptors:
*artery . . . prevention
adult
article
blood flow velocity
clinical trial
color ultrasound flowmetry
controlled study
female
high risk pregnancy: DI, diagnosis
human
low birth weight: PC, prevention

low birth weight: CO, complication
major clinical study
oral drug administration
preeclampsia: PC, prevention
preeclampsia: CO, complication
priority journal
randomized controlled trial
uterine artery
uterus blood flow
*acetylsalicylic acid: CT, clinical trial
*acetylsalicylic acid: DO, drug. . .

L15 ANSWER 39 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95336075 EMBASE
DOCUMENT NUMBER: 1995336075
TITLE: Topical GM1 ganglioside to promote crushed rat sciatic nerve regeneration.
AUTHOR: Wang M.-S.; Chen Z.-W.; Zhang G.-J.; Chen Z.-R.
CORPORATE SOURCE: Department of Orthopaedics, Shanghai Medical University, Zhongshan Hospital,Shanghai 200032, China
SOURCE: Microsurgery, (1995) 16/8 (542-546).
ISSN: 0738-1085 CODEN: MSRGDQ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 009 Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English; Japanese
AB The effects of topical GM1 ganglioside on crushed rat sciatic nerve regeneration were studied in this presentation. Thirty-four rats, with 68 bilateral sciatic nerves, were divided into seven groups: one group of four rats for measurement of normal motor nerve conduction velocity (MNCV), three as controls, and another three in the GM1-treated groups. Sciatic nerves were exposed and crushed at a site 6 mm distal to the sciatic **notch** by the standard technique. In this manner, 3 mm wide crush injuries were created. Then 2.1 .mu.l of normal saline was injected into the crush site in the control groups and an equal volume of GM1 solution (containing 10 .mu.g GM1) was injected into the GM1-treated groups. Electrophysiological, histological, and morphometric evaluations were carried out at 12, 28, and 56 days. A significantly higher muscle action potential (MAP) rate was found in the GM1- treated group (70%) vs. the controls (none) at 12 days ($P < 0.005$), and increased MNCV was found in the GM1-treated groups at both 28 and 56 days, especially at 56 days, when it was 39.59 .+-. 9.23 m/sec vs. 31.42 .+-. 4.07 m/sec in controls ($P < 0.05$). Morphometrically, there were more regenerated myelinated fibers (RMFs) at 12 days, and larger diameter of RMFs were observed at 12, 28, and 56 days in the GM1-treated groups.
SO Microsurgery, (1995) 16/8 (542-546).
ISSN: 0738-1085 CODEN: MSRGDQ
AB . . . three in the GM1-treated groups. Sciatic nerves were exposed and crushed at a site 6 mm distal to the sciatic **notch** by the standard technique. In this manner, 3 mm wide crush injuries were created. Then 2.1 .mu.l of normal saline. . .
CT Medical Descriptors:
*nerve degeneration
*nerve injury: DT, drug therapy
*sciatic nerve
animal tissue
article
crush trauma
morphometrics
muscle action potential
nerve function
nonhuman
priority journal
rat
topical drug administration
***ganglioside gm1: AD, drug administration**
*ganglioside gm1: DT, drug therapy

L15 ANSWER 40 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95322386 EMBASE
DOCUMENT NUMBER: 1995322386
TITLE: Glenoid cysts mimicking cervical radiculopathy.
AUTHOR: Uppal G.S.; Uppal J.A.; Dwyer A.P.
CORPORATE SOURCE: Clinical Faculty, Loma Linda University Medical Center, 6800 Brockton Avenue,Riverside, CA 92506, United States
SOURCE: Spine, (1995) 20/20 (2257-2260).
ISSN: 0362-2436 CODEN: SPINDD
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 008 Neurology and Neurosurgery
033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Study Design. Patients are often referred for the evaluation of neck or radiating shoulder or arm pain who are suspected of having a possible cervical spine origin of their symptoms. Careful evaluation may show ganglion cysts of the glenohumeral joint mimicking symptoms of cervical radiculopathy. Objectives. To present a series of patients in whom cysts originating from the glenohumeral joint caused symptoms mimicking cervical radiculopathy. Summary of Background Data. Suprascapular nerve entrapment in the suprascapular **notch** by ganglion cysts from the glenohumeral joint has been described as the source of vague radicular symptoms. This paper presents a series of patients referred to a spine practice for the evaluation of cervical radiculopathy who actually had glenoid cysts mimicking cervical radiculopathy. Methods. Three hundred forty-two patients were evaluated for cervical radiculopathy; of these, eight had glenoid cysts that were the source of the patients' symptoms. Results. All eight patients had a positive shoulder impingement sign, or, in all, symptoms were temporarily relieved with intra-articular lidocaine injection. Four of the eight patients had abnormal electromyelography and nerve conduction velocity for suprascapular nerve compression. Magnetic resonance imaging of the shoulder was diagnostic in all eight patients. Conclusion. Proper evaluation of the shoulder must be done because it may mimic symptoms of cervical radiculopathy.
SO Spine, (1995) 20/20 (2257-2260).
ISSN: 0362-2436 CODEN: SPINDD
AB . . . originating from the glenohumeral joint caused symptoms mimicking cervical radiculopathy. Summary of Background Data. Suprascapular nerve entrapment in the suprascapular **notch** by ganglion cysts from the glenohumeral joint has been described as the source of vague radicular

symptoms. This paper presents. . .
CT Medical Descriptors:
*cervicobrachial . . . ET, etiology
*cyst: DI, diagnosis
*cyst: SU, surgery
*ganglion
*nerve compression: DI, diagnosis
*shoulder pain: DI, diagnosis
*shoulder pain: ET, etiology
*shoulder pain: DT, drug therapy
adult
clinical article
conference paper
electromyography
excision
female
human
intraarticular drug administration
male
neck pain: DI, diagnosis
neck pain: ET, etiology
neck pain: DT, drug therapy
nerve conduction
nuclear magnetic resonance imaging
priority journal
scapula
*lidocaine: DT, drug. . .

L15 ANSWER 41 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94293078 EMBASE
DOCUMENT NUMBER: 1994293078
TITLE: Vitamin E restores endothelium dependent vasodilatation in cholesterol fed rabbits: In vivo measurements by photoplethysmography.
AUTHOR: Klemsdal T.O.; Andersson T.L.G.; Matz J.; Ferns G.A.A.; Gjesdal K.; Anggard E.L.
CORPORATE SOURCE: William Harvey Research Institute, St Bartholomew's Hospital, Medical College, Carterhouse Square,London EC1M 6BQ, United Kingdom
SOURCE: Cardiovascular Research, (1994) 28/9 (1397-1402).
ISSN: 0008-6363 CODEN: CVREAU
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objective: Pulse curve plethysmography was used to examine the effect of vitamin E on endothelium dependent and independent vasodilatation in unanaesthetised cholesterol fed rabbits in vivo. The height of the dicrotic **notch** was used as an index of general arterial vasodilatation. Methods: Twenty eight rabbits were divided into three study groups; a control group (group 1, n = 8), a group fed 1% cholesterol (group 2, n = 10), and a group fed 1% cholesterol with the addition of 0.2% vitamin E after four weeks (group 3, n = 10). After six weeks on diet the vasodilator responses to acetylcholine and glyceryl trinitrate were measured by photoplethysmography of the rabbit ear. Recordings were made during light sedation at baseline and during infusion of acetylcholine (1.5, 3.0, 6.0, and 12 .mu.g.cntdot.min-1) and glyceryl trinitrate (3.75, 7.5, and 15.0 .mu.g.cntdot.min-1). In a second set of experiments with control fed rabbits (n = 5), acetylcholine infusions were given before and after infusion of L-nitro-arginine (15 mg). Results: The relative height of the dicrotic **notch** (which predominantly indicates arterial tone in the larger vessels) was reduced by acetylcholine in a dose dependent manner, but in cholesterol fed rabbits (group 2) this response was significantly decreased. Rabbits receiving concomitant dietary vitamin E responded in a similar manner to controls. The difference was most prominent using acetylcholine at a dose of 3.0 .mu.g.cntdot.min-1, where the mean change from baseline was 11(SEM 4)% in group 2, compared to 31(6)% in group 1 (p=0.01), and to 26(5)% in group 3 (p=0.02). Similar differences between the groups were observed for the increase in heart rate during acetylcholine infusions. In contrast, the responses to glycelyl trinitrate were similar in all groups. After infusions of L-nitro-arginine, the responses to acetylcholine were blunted. Conclusions: Supplementation with vitamin E restored the otherwise reduced vascular response to acetylcholine in cholesterol fed rabbits. Analysis of photoplethysmographic pulse curves is a simle non-invasive method of evaluating arterial vasodilator effects. However, the nature of the measured dilator response needs to be characterised further.
SO Cardiovascular Research, (1994) 28/9 (1397-1402).
ISSN: 0008-6363 CODEN: CVREAU
AB . . . vitamin E on endothelium dependent and independent vasodilatation in unanaesthetised cholesterol fed rabbits in vivo. The height of the dicrotic **notch** was used as an index of general arterial vasodilatation. Methods: Twenty eight rabbits were divided into three study groups; a. . . 5), acetylcholine infusions were given before and after infusion of L-nitro-arginine (15 mg). Results: The relative height of the dicrotic **notch** (which predominantly indicates arterial tone in the larger vessels) was reduced by acetylcholine in a dose dependent manner, but in. . .
CT Medical Descriptors:
*hypercholesterolemia
*vasodilatation
animal experiment
article
controlled study
intravenous drug administration
male
nonhuman
oral drug administration
plethysmography
priority journal
rabbit
*acetylcholine: PD, pharmacology
*acetylcholine: IT, drug interaction
*acetylcholine: CB, drug combination
*alpha tocopherol: PD, pharmacology
*glyceryl trinitrate: PD, pharmacology
*glyceryl trinitrate: CB,. . .

L15 ANSWER 42 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 94232029 EMBASE
DOCUMENT NUMBER: 1994232029
TITLE: A comparison of the neuromuscular blocking effects of rocuronium bromide at the adductor pollicis and laryngeal adductor muscles.
AUTHOR: Meistelman C.; Plaud B.; Donati F.
CORPORATE SOURCE: Department of Anaesthesia, Institut Gustave Roussy,Villejuif, France
SOURCE: European Journal of Anaesthesiology, Supplement, (1994) 11/9 (33-36).
ISSN: 0952-1941 CODEN: EJSUEP
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 024 Anesthesiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The effects of rocuronium, 0.25 or 0.5 mg kg-1, were measured simultaneously on the adductor muscles of the larynx and adductor pollicis in 14 adult patients. Anaesthesia was induced and maintained with propofol and fentanyl. Tracheal intubation was performed without muscle relaxants. The recurrent laryngeal and ulnar nerves were both stimulated supramaximally, at the **notch** of the thyroid cartilage and at the wrist respectively, using train-of-four stimulation. The laryngeal response was evaluated by measuring the pressure change in the cuff of a tracheal tube positioned between the vocal cords. Onset time, intensity of blockade and duration of action were less at the larynx than at the adductor pollicis. After rocuronium, 0.25 mg kg-1, the onset time (interval between injection and maximal T1 blockade) was 1.6 .+-. 0.1 min and 3.0 .+-. 0.3 min (mean .+-. SEM) at the laryngeal muscles and adductor pollicis, respectively (P < 0.01 between muscles). Maximum blockade was 37 .+-. 8% and 69 .+-. 8%, respectively (P < 0.05), and time to 90 T1 recovery was 7 .+-. 1 min and 20 .+-. 4 min, respectively (P < 0.05). With 0.5 mg kg-1, the onset time was also more rapid at the vocal cords (1.4 .+-. 0.1 min) than at the adductor pollicis (2.4 .+-. 0.2 min, P < 0.001). Maximum blockade was 77 .+-. 5% and 98 .+-. 1%, respectively (P < 0.01), and time to 90% T1 recovery was 22 min.

SO European Journal of Anaesthesiology, Supplement, (1994) 11/9 (33-36).
ISSN: 0952-1941 CODEN: EJSUEP

AB . . . fentanyl. Tracheal intubation was performed without muscle relaxants. The recurrent laryngeal and ulnar nerves were both stimulated supramaximally, at the **notch** of the thyroid cartilage and at the wrist respectively, using train-of-four stimulation. The laryngeal response was evaluated by measuring the. . .

CT Medical Descriptors:
*larynx muscle
*neuromuscular blocking
*skeletal muscle
adult
clinical article
clinical trial
conference paper
drug activity
drug effect
endotracheal intubation
endotracheal tube
general anesthesia
human
intravenous drug administration
laryngeal nerve
nerve stimulation
ulnar nerve
vocal cord
*rocuronium
fentanyl
neuromuscular blocking agent
propofol

L15 ANSWER 43 OF 90 EMBASE
ACCESSION NUMBER: 94098839 EMBASE
DOCUMENT NUMBER: 1994098839
TITLE: Evaluation of the effects of nasal decongestants with acoustic rhinometry.
AUTHOR: Tanaka T.; Okita W.; Kase Y.; Inuma T.
CORPORATE SOURCE: Department of Otorhinolaryngology, Tokyo University Branch Hospital,Tokyo, Japan
SOURCE: Journal of Otolaryngology of Japan, (1994) 97/2 (207-212).
ISSN: 0030-6622 CODEN: JOJAA6
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 011 Otorhinolaryngology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English

AB Acoustic rhinometry is a new method of evaluating the geometrical distributions of the cross-section and volume of the nasal cavity. Its characteristics are that of a nontraumatic procedure requiring minimal time for measurements. Eight males (27-39 years old) without nasal lesions were investigated with acoustic rhinometry before and after unilateral **administrations** of decongestants. Conventional nasal decongestants such as naphazolin nitrate 0.1% (Privina) and tetrahydrozoline hydrochloride 0.1% as well as prednisolone 0.02% (Cor-tyzine), were used in solutions diluted 10 or 100 times. As to the method of decongestant application, we adopted the head tilt method, in the successive order of backward, lateral (toward the non-application side) tilt and backward. Each position was maintained for 30 seconds. Minimal cross sectional area of the nasal cavity, and nasal volume were evaluated with acoustic rhinometry. After the application of nasal drops, the minimal cross sectional area increased within 10 minutes, followed by a plateau level for one hour. With the application of nasal decongestants, an 1-**notch**, corresponding to the nasal valve, was unchanged, whereas the C-**notch**, corresponding to the anterior and of the inferior turbinate, often shifted upwards. Thus, the minimal cross sectional area changed from an 1-**notch** to a C-**notch** location. The volume of the nasal cavity increased within 10 minutes, and maintained a plateau level for one hour which was similar to that of the minimal cross sectional area. Changes in the ratio of the minimal cross sectional area were greater for less diluted solutions. Changes in the ratio of the nasal cavity were similar to those of the minimal cross sectional area.

SO Journal of Otolaryngology of Japan, (1994) 97/2 (207-212).
ISSN: 0030-6622 CODEN: JOJAA6
AB . . . time for measurements. Eight males (27-39 years old) without nasal lesions were investigated with acoustic rhinometry before and after unilateral **administrations** of decongestants. Conventional nasal decongestants such as naphazolin nitrate 0.1% (Privina) and tetrahydrozoline hydrochloride 0.1% as well as prednisolone 0.02%. . . area increased within 10 minutes, followed by a plateau level for one hour. With the application of nasal decongestants, an 1-**notch**, corresponding to the nasal valve, was unchanged, whereas the C-**notch**, corresponding to the anterior and of the inferior turbinate, often shifted upwards. Thus, the minimal cross sectional area changed from an 1-**notch** to a C-**notch** location. The volume of the nasal cavity increased within 10 minutes, and maintained a plateau level for one hour which. . .
CT Medical Descriptors:
*acoustics
adult
article
clinical article
drug effect
human
intranasal drug administration
male
nose cavity
*decongestive agent: PD, pharmacology
*naphazoline: PD, pharmacology
*prednisolone: PD, pharmacology
*tetryzoline: PD, pharmacology
cortyzine
unclassified drug

L15 ANSWER 44 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93329722 EMBASE
DOCUMENT NUMBER: 1993329722
TITLE: [Monitoring neuromuscular function: Capnography versus relaxometry].
UBERWACHUNG DER NEUROMUSKULAREN FUNKTION: KAPNOGRAPHIE VERSUS RELAXOMETRIE.
AUTHOR: Bissinger U.; Lenz G.; Reiter A.; Albrecht T.; Schorer R.
CORPORATE SOURCE: Klin fur Anasthesiol/Transfusionmed., Abteilung fur Anasthesiologie, Universitat Tubingen, Hoppe-Seyler-Strasse 3,72076 Tubingen, Germany
SOURCE: Anasthesiologie Intensivmedizin Notfallmedizin Schmerztherapie, (1993) 28/6 (359-362).
ISSN: 0939-2661 CODEN: AISTE5
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 024 Anesthesiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: English; German
AB Objective: A **notch** ('curare cleft') in the plateau phase of the capnogram of the ventilated patient has been presumed to be a typical early sign of the fading effect of muscle relaxants on the diaphragm. For that reason a prospective study was done to investigate whether capnography can be used diagnostically to indicate the fading effect of vecuronium confirmed by peripheral relaxometry. Methods: Twenty-five consecutive patients who received inhalation anaesthesia with isoflurane, N2O/O2, and vecuronium during elective neurosurgical procedures were studied. Whenever intraoperative 'curare clefts' appeared in the capnogram, diaphragm activity was measured and a simultaneous relaxogram of the adductor pollicis muscle was recorded. After every such event, vecuronium was readministered for complete relaxation. Results: A deformation of the capnogram was registered in 17/25 patients and in all instances (51/51) was caused by diaphragm activity. The deformation disappeared after renewed relaxation and was therefore a reliable indicator of spontaneous breathing. However, it did not correlate with the degree of relaxation of peripheral muscles, because diaphragm activity was present during all degrees of peripheral relaxation, but could also be absent even after complete recovery of neuromuscluar transmission. Conclusion: Capnography is therefore not a reliable method to indicate the fading effect of muscle relaxants.
SO Anasthesiologie Intensivmedizin Notfallmedizin Schmerztherapie, (1993) 28/6 (359-362).
ISSN: 0939-2661 CODEN: AISTE5
AB Objective: A **notch** ('curare cleft') in the plateau phase of the capnogram of the ventilated patient has been presumed to be a typical. .
CT Medical Descriptors:
*capnography
*muscle relaxation
*neuromuscular blocking
adult
aged
article
clinical article
human
inhalational drug administration
*vecuronium
isoflurane
nitrous oxide

L15 ANSWER 45 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93221820 EMBASE
DOCUMENT NUMBER: 1993221820
TITLE: Relationship between mean arterial pressure and parameters derived from blood flow velocity waveforms in the systemic circulation of fetal sheep.
AUTHOR: Muijsers G.J.J.M.; Van Huisseling A.; Hasaart T.H.M.
CORPORATE SOURCE: Dept of Obstetrics and Gynecology, Academic Hospital Masstricht, PO Box 5800,NL-6202 AZ Maastricht, Netherlands
SOURCE: Gynecologic and Obstetric Investigation, (1993) 36/1 (1-7).
ISSN: 0378-7346 CODEN: GOBIDS
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In 8 fetal sheep under anesthesia, we examined the relationship between

the fetal aorta blood flow velocity waveform and fetal mean arterial pressure after **administration** of norepinephrine and angiotensin II. It was hypothesized that the pulsatility index (PI) of the waveform would change during fetal hypertension. Measurements were performed using a 20-MHz Doppler transducer on the aorta directly beneath the diaphragm and a catheter inserted via the femoral artery into the abdominal aorta. Further instrumentation included a Doppler transducer and an electromagnetic flowmeter on the common umbilical artery and a catheter in the inferior vena cava. Fetal hypertension was induced by bolus **administration** of either norepinephrine or angiotensin II or by infusion of norepinephrine. With the Doppler transducer on the common umbilical artery, it was possible to study external iliac artery blood velocity waveforms in 4 fetal lambs, whereas aorta blood velocity waveforms were recorded in 7 fetal lambs. The measurements of external iliac artery PI and mean arterial pressure were characterized by a linear regression with a correlation coefficient of 0.72, whereas the measurements of aorta PI and mean arterial blood pressure were characterized by a linear regression with a correlation coefficient of 0.40. However, notable changes were observed in the aorta blood velocity waveform, which were not expressed by a substantial increase in the aorta PI. These changes can be described as a narrowing of the systolic peak and an earlier occurrence of the first dicrotic **notch**. The correlation coefficient of the linear regression between the cardiac cycle time until occurrence of the first dicrotic **notch** in the aorta blood velocity waveform and mean arterial blood pressure was -0.77. It is concluded that, in fetal sheep, the aorta blood velocity waveforms change in response to **administration** of hypertensive drugs.

SO Gynecologic and Obstetric Investigation, (**1993**) 36/1 (1-7).
ISSN: 0378-7346 CODEN: GOBIDS

AB . . . under anesthesia, we examined the relationship between the fetal aorta blood flow velocity waveform and fetal mean arterial pressure after **administration** of norepinephrine and angiotensin II. It was hypothesized that the pulsatility index (PI) of the waveform would change during fetal. . . flowmeter on the common umbilical artery and a catheter in the inferior vena cava. Fetal hypertension was induced by bolus **administration** of either norepinephrine or angiotensin II or by infusion of norepinephrine. With the Doppler transducer on the common umbilical artery,. . . These changes can be described as a narrowing of the systolic peak and an earlier occurrence of the first dicrotic **notch**. The correlation coefficient of the linear regression between the cardiac cycle time until occurrence of the first dicrotic **notch** in the aorta blood velocity waveform and mean arterial blood pressure was -0.77. It is concluded that, in fetal sheep, the aorta blood velocity waveforms change in response to **administration** of hypertensive drugs.

L15 ANSWER 46 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93215115 EMBASE
DOCUMENT NUMBER: 1993215115
TITLE: Postoperative pain after anterior cruciate ligament reconstruction using a transligamentous approach.
AUTHOR: Solheim E.; Strand T.
CORPORATE SOURCE: Department of Orthopedics, Haukeland Hospital, University of Bergen,N-5021 Bergen, Norway
SOURCE: American Journal of Sports Medicine, (**1993**) 21/4 (507-509).
ISSN: 0363-5465 CODEN: AJSMDO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Anterior cruciate ligament reconstruction by free patellar tendon graft was performed using 2 different surgical approaches to the intercondylar **notch** in 67 consecutive patients with chronic anterior cruciate ligament insufficiency. In the first 30 patients (Group A), the traditional medial parapatellar arthrotomy with lateral luxation of the patella was done, whereas in the last 37 patients (Group B) a transpatellar tendon approach was used. Postoperative pain was managed by analgesics and, in patients who had epidural anesthesia, by **administration** of bupivacaine in indwelling catheters. Generally, the analgesics and bupivacaine were given immediately on request to establish comfort at rest and to permit range of motion exercises without severe pain. Compared with those in Group A, the patients of Group B had a significantly longer period from the first dose of analgesic or bupivacaine to the second, and the total number of doses of analgesic or bupivacaine was significantly lower. In the subgroup of patients with epidural anesthesia (21 in Group A and 32 in Group B), the Group B patients required significantly less analgesics, as doses equivalent to 10 mg of morphine, compared with that of Group A.

SO American Journal of Sports Medicine, (**1993**) 21/4 (507-509).
ISSN: 0363-5465 CODEN: AJSMDO

AB Anterior cruciate ligament reconstruction by free patellar tendon graft was performed using 2 different surgical approaches to the intercondylar **notch** in 67 consecutive patients with chronic anterior cruciate ligament insufficiency. In the first 30 patients (Group A), the traditional medial. . . a transpatellar tendon approach was used. Postoperative pain was managed by analgesics and, in patients who had epidural anesthesia, by **administration** of bupivacaine in indwelling catheters. Generally, the analgesics and bupivacaine were given immediately on request to establish comfort at rest. . .

CT Medical Descriptors:
*anterior cruciate ligament
*ligament surgery
*postoperative pain: DT, drug therapy
*postoperative pain: CO, complication
adolescent
adult
arthrotomy
article
epidural anesthesia
female
human
intramuscular drug administration
major clinical study
male
mobilization
postoperative analgesia
priority journal
surgical approach
tendon graft
*analgesic agent: DO, drug dose

*analgesic agent: DT, drug therapy
***bupivacaine: AD, drug administration**
*bupivacaine: DO, drug dose
*bupivacaine: DT, drug therapy
codeine: DO, drug dose
codeine: CB, drug combination
codeine: DT, drug therapy
morphine: DT, drug therapy
morphine: AD, drug administration
paracetamol: CB, drug combination
paracetamol: DO, drug dose
paracetamol: DT, drug therapy
pethidine: DT, drug therapy
pethidine: AD, drug administration

L15 ANSWER 47 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93211247 EMBASE
DOCUMENT NUMBER: 1993211247
TITLE: Spectral Doppler flow profiles in neonates with obstructive lesions of the aortic arch.
AUTHOR: Sreeram N.; Walsh K.; Jackson M.
CORPORATE SOURCE: Heart Clinic, Royal Liverpool Children's Hospital, Eaton Road,Liverpool L12 2AP, United Kingdom
SOURCE: International Journal of Cardiology, (1993) 40/2 (101-110).
ISSN: 0167-5273 CODEN: IJCDD5
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The aim was to assess the value of continuous and pulsed wave Doppler ultrasound in the detection and differentiation of obstructive lesions of the aortic arch in neonates. In 31 neonates with proven arch obstruction (pre- or juxtaductal coarctation in 19 patients; postductal coarctation in five patients; interrupted aortic arch in four patients; aortic arch atresia in three patients), continuous wave Doppler interrogation of the descending aorta from the suprasternal **notch** revealed a high velocity jet (greater than 2.2 m/s) directed away from the transducer in 12 patients. Of these, four neonates had preductal coarctation, and five postductal coarctation. The remaining three patients had arch interruption or atresia. Image guided pulsed Doppler ultrasound recordings were obtained from the arch upstream from the obstruction, the descending aorta distal to the obstruction, and from the arterial duct. Patients with coarctation had a prominent diastolic flow directed away from the transducer in the arch upstream from the obstruction, representing a diastolic coarctation gradient, or diastolic steal either by the patent arterial duct or by collateral vessels. In contrast, patients with arch interruption or atresia had only a systolic flow signal in the proximal arch. Ductal flow was either bidirectional (preductal coarctation, arch interruption, arch atresia), continuous right to left flow from pulmonary artery to aorta (one case each of juxtaductal coarctation and arch atresia), or continuous left to right flow from aorta to pulmonary artery (postductal coarctation). In neonates wide patency of the duet often precludes the development of a large pressure drop across a coarctation. Conversely a high velocity signal may be recorded from a patent but restrictive duct. In conjunction with imaging, pulsed Doppler velocity profiles from the arch and patent duct permit a meaningful interpretation of the haemodynamics of arch obstruction.
SO International Journal of Cardiology, (1993) 40/2 (101-110).
ISSN: 0167-5273 CODEN: IJCDD5
AB . . . in four patients; aortic arch atresia in three patients), continuous wave Doppler interrogation of the descending aorta from the suprasternal **notch** revealed a high velocity jet (greater than 2.2 m/s) directed away from the transducer in 12 patients. Of these, four. . .
CT Medical Descriptors:
*aorta coarctation: DI, diagnosis
*aorta coarctation: DT, drug therapy
*aorta occlusion: DI, diagnosis
*echography
article
clinical article
doppler flowmetry
female
hemodynamics
human
intravenous drug administration
male
newborn
priority journal
prostaglandin e2: DT, drug therapy

L15 ANSWER 48 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92310026 EMBASE
DOCUMENT NUMBER: 1992310026
TITLE: Rocuronium (ORG 9426) neuromuscular blockade at the adductor muscles of the larynx and adductor pollicis in humans.
AUTHOR: Meistelman C.; Plaud B.; Donati F.
CORPORATE SOURCE: Department of Anaesthesia, Royal Victoria Hospital, 687 Pine Avenue West,Montreal, Que. H3A 1A1, Canada
SOURCE: Canadian Journal of Anaesthesia, (1992) 39/7 (665-669).
ISSN: 0832-610X CODEN: CJOAEP
COUNTRY: Canada
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 024 Anesthesiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English; French
AB The effects of rocuronium, 0.25 or 0.5 mg.cntdot.kg-1, were measured simultaneously on the adductor muscles of the larynx and adductor pollicis in 14 adult patients. Anaesthesia was induced and maintained with propofol and fentanyl. Tracheal intubation was performed without muscle relaxants. The recurrent laryngeal and ulnar nerves were both stimulated supramaximally, at the **notch** of the thyroid cartilage and at the wrist respectively, using train-of-four stimulation. The laryngeal response was evaluated by measuring the pressure change in the cuff of a tracheal tube positioned between the vocal cords. Onset time, intensity of

blockade and duration of action were less at the larynx than at the adductor pollicis. After rocuronium, 0.25 mg.cntdot.kg-1, the onset time (interval between injection and maximal T1 blockade) was 1.6 .+-. 0.1 min and 3.0 .+-. 0.3 min (mean .+-. SEM) at the laryngeal muscles and adductor pollicis, respectively (P < 0.01 between muscles). Maximum blockade was 37 .+-. 8% and 69 .+-. 8%, respectively (P < 0.05), and time to 90% T1 recovery was 7 .+-. 1 min and 20 .+-. 4 min, respectively (P < 0.05). With 0.5 mg.cntdot.kg-1, the onset time was also more rapid at the vocal cords (1.4 .+-. 0.1 min) than at the adductor pollicis (2.4 .+-. 0.2 min, P < 0.001). Maximum blockade was 77 .+-. 5% and 98 .+-. 1%, respectively (P < 0.01), and time to 90% T1 recovery was 22 .+-. 3 min and 37 .+-. 4 min, respectively (P < 0.01). It is concluded that with rocuronium onset and recovery are faster at the laryngeal adductor muscles, but blockade is less intense than at the adductor pollicis. These findings are similar to the observations made previously with vecuronium, except that rocuronium had a faster onset at both muscles.

SO Canadian Journal of Anaesthesia, (**1992**) 39/7 (665-669).
ISSN: 0832-610X CODEN: CJOAEP

AB . . . fentanyl. Tracheal intubation was performed without muscle relaxants. The recurrent laryngeal and ulnar nerves were both stimulated supramaximally, at the **notch** of the thyroid cartilage and at the wrist respectively, using train-of-four stimulation. The laryngeal response was evaluated by measuring the. . .

CT Medical Descriptors:
*muscle relaxation
*neuromuscular blocking
adult
article
clinical article
human
intravenous drug administration
larynx
priority journal
*neuromuscular blocking agent
1 (17beta acetoxy 3alpha hydroxy 2beta morpholino 5alpha androstan 16beta yl) 1 allylpiperidinium bromide
rocuronium: PD,. . .

L15 ANSWER 49 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92293767 EMBASE
DOCUMENT NUMBER: 1992293767
TITLE: Effects of graded vasoconstriction upon the measurement of finger arterial pressure.
AUTHOR: Imholz B.P.M.; Parati G.; Mancia G.; Wesseling K.H.
CORPORATE SOURCE: Department of Internal Medicine, Academic Medical Centre, Meibergdreef 9,1105 AZ Amsterdam, Netherlands
SOURCE: Journal of Hypertension, (**1992**) 10/9 (979-984).
ISSN: 0263-6352 CODEN: JOHYD3
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Objective: To assess the effects of incremental phenylephrine infusion rates and subsequent graded vasoconstriction upon the performance of the Ohmeda Finapres. Design: Blood pressure in eight hypertensive patients in the finger and the brachial artery was recorded simultaneously. Systolic blood pressure (SBP), diastolic blood pressure (DPB) and mean arterial pressure (MAP) were compared as well as additional waveform characteristics like the pressure at moment of the dicrotic **notch** and calculation of the pulsatile-systolic areas. Results: Before phenylephrine infusion SBP and DBP were higher in the finger. At maximal infusion (1.6 .mu.g/kg/min) the increase in brachial SBP was significantly underestimated by Finapres. Thus, the computed sensitivities of baroreflex control for SBP differed significantly between the two measurements. Under control conditions, the shape of the finger waveform differed from the brachial-artery waveform in terms of: (1) a more peaked appearance; (2) a dicrotic **notch** (P(**notch**)) which is located at a lower percentage of pulse pressure; and (3) a larger pulsatile-systolic area. At maximal infusion rates finger P(**notch**) increased whilst intrabrachial P(**notch**) did not. In contrast, the brachial and finger pulsatile-systolic areas changed fully in parallel. Conclusions: Phenylephrine infusion caused a significant, and clinically important, underestimation of the increase in brachial SBP when assessed by Finapres, whereas MAP and DBP and pulsatile-systolic area track intra-arterial pressure reliably.

SO Journal of Hypertension, (**1992**) 10/9 (979-984).
ISSN: 0263-6352 CODEN: JOHYD3

AB . . . mean arterial pressure (MAP) were compared as well as additional waveform characteristics like the pressure at moment of the dicrotic **notch** and calculation of the pulsatile-systolic areas. Results: Before phenylephrine infusion SBP and DBP were higher in the finger. At maximal. . . of the finger waveform differed from the brachial-artery waveform in terms of: (1) a more peaked appearance; (2) a dicrotic **notch** (P(**notch**)) which is located at a lower percentage of pulse pressure; and (3) a larger pulsatile-systolic area. At maximal infusion rates finger P(**notch**) increased whilst intrabrachial P(**notch**) did not. In contrast, the brachial and finger pulsatile-systolic areas changed fully in parallel. Conclusions: Phenylephrine infusion caused a significant,. . .

CT Medical Descriptors:
*arterial pressure
*blood pressure measurement
*digital artery
*vasoconstriction
article
brachial artery
clinical article
controlled study
diastolic blood pressure
drug effect
human
intermethod comparison
intravenous drug administration
mean arterial pressure
pressoreceptor reflex
reliability
systolic blood pressure
waveform
*phenylephrine: DO, drug dose
*phenylephrine: PD, pharmacology

L15 ANSWER 50 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92199094 EMBASE
DOCUMENT NUMBER: 1992199094
TITLE: Elucidating the vascular response to burns with a new rat model.
AUTHOR: Regas F.C.; Ehrlich H.P.
CORPORATE SOURCE: Shriners Burns Institute, 51 Blossom St.,Boston, MA 02114, United States
SOURCE: Journal of Trauma, (1992) 32/5 (557-563).
ISSN: 0022-5282 CODEN: JOTRA5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
037 Drug Literature Index
049 Forensic Science Abstracts
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Burn injury causes acute thrombosis and occlusion of vessels in the dermis directly killed by thermal energy. A vascular response also occurs in the uninjured dermis bordering the site of injury. Diminished blood flow leads to progressive ischemia and necrosis in the dermis beneath and surrounding the burn. If blood flow is maintained or restored in this area, the tissue survives. A noninvasive technique for studying dynamic changes in blood flow in this transitional dermis in rats is presented. A rectangular brass bar 19 mm wide with 5-mm transverse **notches** was heated in boiling water and applied to the skin surface for 20 seconds, making a 'comb' burn composed of a row of four rectangular 10 x 19-mm full-thickness burns. Between the burns were 5 x 19-mm bands of uninjured skin, called 'interspaces.' After burning, blood flow near the surface of both the burn sites and the interspaces was monitored with a laser Doppler perfusion monitor for 24 hours. The vascular patency of blood vessels was directly visualized by latex vascular casts made 24 hours after burn. The possible prevention of progressive ischemia by injecting systemic ibuprofen was examined in this new model. Normal skin has a surface blood flow reading of 80 .+-. 16 mV, burn sites have a reading of 11 .+-. 4 mV, and interspaces have a reading of 21 .+-. 4 mV at 24 hours postburn in untreated rats. Systemic ibuprofen given IM immediately postburn at 12.5 mg/kg increased blood flow to 80 .+-. 28 mV within the interspaces, to 17 .+-. 12 mV in the burn site, and to 80 .+-. 9 mV in normal skin. The vascular casts showed an absence of patent vessels within both the burn sites and interspaces in untreated rats. The four individual burn sites had generated into a larger single full-thickness injury. In treated rats patent vessels were present in the interspaces but not in the burn sites. Four individual wounds were evident at 24 hours. Histologic preparations of vascular casts showed the absence of latex-filled vessels and thrombus-filled vessels in the burn sites and the interspaces of untreated rats. With ibuprofen therapy, latex-filled vessels were evident within the interspaces and dermis as were thrombus-filled vessels within the burn sites.
SO Journal of Trauma, (1992) 32/5 (557-563).
ISSN: 0022-5282 CODEN: JOTRA5
AB . . . blood flow in this transitional dermis in rats is presented. A rectangular brass bar 19 mm wide with 5-mm transverse **notches** was heated in boiling water and applied to the skin surface for 20 seconds, making a 'comb' burn composed of. . .
CT Medical Descriptors:
*blood vessel reactivity
*burn
animal experiment
animal model
animal tissue
article
blood vessel diameter
blood vessel occlusion: ET, etiology
controlled study
dermis
drug effect
intramuscular drug administration
ischemia: ET, etiology
ischemia: PC, prevention
laser doppler flowmetry
male
nonhuman
priority journal
rat
skin blood flow
thrombosis: ET, etiology
*ibuprofen
latex

L15 ANSWER 51 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92019471 EMBASE
DOCUMENT NUMBER: 1992019471
TITLE: Cutaneous Pneumocystis carinii infection in patients with acquired immunodeficiency syndrome.
AUTHOR: Hennessey N.P.; Parro E.L.; Cockerell C.J.
CORPORATE SOURCE: Division of Dermatopathology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75235-9072, United States
SOURCE: Archives of Dermatology, (1991) 127/11 (1699-1701).
ISSN: 0003-987X CODEN: ARDEAC
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
013 Dermatology and Venereology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Extrapulmonary infection with Pneumocystis carinii is an uncommon event in which the skin may be affected rarely. All cases heretofore described in immunocompromised hosts have involved the external auditory canal and mastoid areas. We describe two patients with acquired immunodeficiency syndrome and extrapulmonary cutaneous P carinii infection that involved the glabrous skin. The first was a 31-year-old white man seropositive for human immunodeficiency virus with prior episodes of P carinii pneumonia and infection with Mycobacterium avium-intracellulare evaluated for translucent papules on the skin with an appearance similar to molluscum contagiosum infection. Biopsy confirmed the diagnosis of cutaneous pneumocystosis. The second patient was a 36-year-old homosexual man with long-standing liver disease with a persistent cough, fever, and an

abnormal chest roentgenogram. Cutaneous evaluation revealed a bluish macule on the sternal **notch** that on skin biopsy was diagnostic of cutaneous pneumocystosis. Treatment with intravenous pentamidine resulted in resolution of the pulmonary and cutaneous problems in both cases. Extrapulmonary P carinii infection may involve the skin at sites other than the external auditory canal and may have a nondescript appearance. Histologic findings are similar to those of pneumocystosis found elsewhere. Clinicians should be familiar with the nondescript nature of the eruption as skin biopsy may be helpful in establishing a diagnosis of systemic pneumocystosis.

SO Archives of Dermatology, (**1991**) 127/11 (1699-1701).
ISSN: 0003-987X CODEN: ARDEAC

AB . . . disease with a persistent cough, fever, and an abnormal chest roentgenogram. Cutaneous evaluation revealed a bluish macule on the sternal **notch** that on skin biopsy was diagnostic of cutaneous pneumocystosis. Treatment with intravenous pentamidine resulted in resolution of the pulmonary and. . .

CT Medical Descriptors:
*acquired immune deficiency syndrome
*pneumocystis carinii pneumonia: DT, drug therapy
*pneumocystis carinii pneumonia: DI, diagnosis
*skin infection: DT, drug therapy
*skin infection: DI, diagnosis
adult
article
case report
human
inhalational drug administration
intravenous drug administration
male
mycobacterium intracellulare avium
priority journal
*pentamidine: DT, drug therapy

L15 ANSWER 52 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 91283258 EMBASE
DOCUMENT NUMBER: 1991283258
TITLE: Neuromuscular effects of succinylcholine on the vocal cords and adductor pollicis muscles.
AUTHOR: Meistelman C.; Plaud B.; Donati F.
CORPORATE SOURCE: Department of Anesthesiology, Royal Victoria Hospital, 687 Pine Avenue West,Montreal, Que. H3A 1A1, Canada
SOURCE: Anesthesia and Analgesia, (**1991**) 73/3 (278-282).
ISSN: 0003-2999 CODEN: AACRAT
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 024 Anesthesiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB To quantify the effects of succinylcholine at the laryngeal adductor muscles and the adductor pollicis, 17 adult patients were studied during propofol-fentanyl anesthesia. Train-of-four stimulation was applied to the ulnar nerve at the wrist and the recurrent laryngeal nerve at the **notch** of the thyroid cartilage. Laryngeal response was measured as pressure changes in the cuff of the tracheal tube positioned between the vocal cords. The force of contraction of the laryngeal adductor muscles and of the adductor pollicis were compared after **administration** of 0.25 or 0.5 mg/kg of succinylcholine. With 0.25 mg/kg, maximum blockade of first twitch (T1) was 66% .+-. 10% (mean .+-. SEM) and 45% .+-. 13% at the vocal cords and the adductor pollicis, respectively ($P < 0.01$). After 0.5 mg/kg, maximum blockade at the vocal cords (93% .+-. 2%) and the adductor pollicis (84% .+-. 6%) did not differ significantly. For both doses, time to maximal blockade was shorter for the vocal cords (0.9 .+-. 0.1 min) than for the adductor pollicis (1.7 .+-. 0.2 min; $P < 0.01$). Time to 90% recovery of T1 after a bolus of 0.5 mg/kg was similar at the vocal cords (4.3 .+-. 0.5 min) and the adductor pollicis (5.2 .+-. 0.8 min) (NS). The ED50 was less at the laryngeal adductors (0.170 mg/kg) than at the adductor pollicis (0.278 mg/kg). It is concluded that, in adults, succinylcholine-induced blockade is more rapid and more intense at the laryngeal muscles than at the adductor pollicis.

SO Anesthesia and Analgesia, (**1991**) 73/3 (278-282).
ISSN: 0003-2999 CODEN: AACRAT

AB . . . propofol-fentanyl anesthesia. Train-of-four stimulation was applied to the ulnar nerve at the wrist and the recurrent laryngeal nerve at the **notch** of the thyroid cartilage. Laryngeal response was measured as pressure changes in the cuff of the tracheal tube positioned between. . . the vocal cords. The force of contraction of the laryngeal adductor muscles and of the adductor pollicis were compared after **administration** of 0.25 or 0.5 mg/kg of succinylcholine. With 0.25 mg/kg, maximum blockade of first twitch (T1) was 66% .+-. 10%. . . .

CT Medical Descriptors:
*muscle relaxation
*neuromuscular blocking
*vocal cord
adult
aged
article
clinical article
controlled study
human
intravenous drug administration
larynx
priority journal
trachea
*suxamethonium: PD, pharmacology
*suxamethonium: DO, drug dose

L15 ANSWER 53 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 91259121 EMBASE
DOCUMENT NUMBER: 1991259121
TITLE: Vecuronium neuromuscular blockade at the adductor muscles of the larynx and adductor pollicis.
AUTHOR: Donati F.; Meistelman C.; Plaud B.
CORPORATE SOURCE: Department of Anaesthesia, Royal Victoria Hospital, 687 Pine Avenue West, Montreal, Que., H3A 1A1, Canada
SOURCE: Anesthesiology, (**1991**) 74/5 (833-837).
ISSN: 0003-3022 CODEN: ANESAV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 024 Anesthesiology
030 Pharmacology

037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The differences between neuromuscular blockade of the adductor muscles of the vocal cords and the adductor pollicis were examined in 20 adult women anesthetized with fentanyl and propofol. Vecuronium 0.04 or 0.07 mg/kg was given as a single bolus by random allocation. The force of contraction of the adductor pollicis was recorded. Laryngeal response was measured as pressure changes in the cuff of the tracheal tube positioned between the vocal cords. Train-of-four stimulation was applied to the recurrent laryngeal nerve at the **notch** of the thyroid cartilage and to the ulnar nerve at the wrist. Neuromuscular blockade had a faster onset, was less intense, and recovered more rapidly at the vocal cords. With 0.04 mg/kg, maximum blockade of first twitch (T1) was 55 .+-. 8 (mean .+-. standard error of the mean [SEM]) and 88 .+-. 4% at the vocal cords and the adductor pollicis, respectively (P = 0.006). Onset time was 3.3 .+-. 0.1 and 5.7 .+-. 0.2 min, respectively (P = 0.000001), and time to 90% T1 recovery was 11.3 .+-. 1.6 and 26.1 .+-. 1.8 min, respectively (P = 0.001). With 0.07 mg/kg, onset time was unchanged; maximum blockade was more intense, being 88 .+-. 4 and 98 .+-. 1%, respectively (P = 0.04 between muscles); and time to 90% T1 recovery was 23.3 .+-. 1.8 min at the vocal cords versus 40.3 .+-. 2.9 min at the adductor pollicis (P = 0.001). Approximately 1.73 times as much vecuronium was required at the larynx compared with the dose required at the adductor pollicis for the same intensity of blockade. It is concluded that total relaxation of the vocal cords requires large doses of vecuronium, but that maximum effect is reached more rapidly than at the adductor pollicis.
SO Anesthesiology, (**1991**) 74/5 (833-837).
ISSN: 0003-3022 CODEN: ANESAV
AB . . . of the tracheal tube positioned between the vocal cords. Train-of-four stimulation was applied to the recurrent laryngeal nerve at the **notch** of the thyroid cartilage and to the ulnar nerve at the wrist. Neuromuscular blockade had a faster onset, was less. . .
CT Medical Descriptors:
*larynx
*muscle relaxation
*neuromuscular blocking
article
cartilage
clinical article
female
human
intravenous drug administration
priority journal
thyroid gland
*vecuronium: PD, pharmacology
*vecuronium: DT, drug therapy
fentanyl: DT, drug therapy
propofol: DT, drug therapy

L15 ANSWER 54 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 91259120 EMBASE
DOCUMENT NUMBER: 1991259120
TITLE: A method to measure elicited contraction of Laryngeal adductor muscles during anesthesia.
AUTHOR: Donati F.; Plaud B.; Meistelman C.
CORPORATE SOURCE: Department of Anaesthesia, Royal Victoria Hospital, 687 Pine Avenue West, Montreal, Que., H3A 1A1, Canada
SOURCE: Anesthesiology, (**1991**) 74/5 (827-832).
ISSN: 0003-3022 CODEN: ANESAV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 024 Anesthesiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The recurrent laryngeal nerve was stimulated with surface electrodes to produce vocal cord adduction, and the response was measured as pressure changes in the inflatable cuff of a tracheal tube positioned between the vocal cords. To test the linearity of the system, a model of the larynx consisting of a syringe barrel was constructed, and weights were applied to two bands of tissue simulating the vocal cords. Tests on Mallinckrodt size-7.5 tubes showed that the pressure increase produced by a given force was independent of baseline pressure in the range 10-30 mmHg. In addition, the pressure inside the inflatable cuff was linear with increasing weight (or force) for a baseline pressure of 10 mmHg. Thirty ASA physical status 1 or 2 adults were anesthetized with propofol and fentanyl. Tracheal intubation was performed in the absence of muscle relaxants, and the inflatable cuff of the tracheal tube was positioned between the vocal cords. Pressure inside the cuff was measured with an air-filled transducer. Stimulation was produced at different sites along the course of the recurrent laryngeal nerve. A surface electrode placed over the **notch** of the thyroid cartilage produced consistent adduction of the cords, measured as an increase of 8.9 .+-. 5.1 mmHg (mean .+-. standard deviation [SD]) in the cuff pressure. Neuromuscular blocking drugs produced train-of-four fade, and large doses abolished the response completely, ruling out direct muscle stimulation. It is concluded that this assembly can provide useful information on intrinsic laryngeal muscle function.
SO Anesthesiology, (**1991**) 74/5 (827-832).
ISSN: 0003-3022 CODEN: ANESAV
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CT Medical Descriptors:
*laryngeal nerve
*larynx
*neuromuscular synapse
*vocal cord
article
clinical article
human
intravenous drug administration
neuromuscular blocking
priority journal
*fentanyl: DT, drug therapy
*propofol: DT, drug therapy

L15 ANSWER 55 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90258546 EMBASE
DOCUMENT NUMBER: 1990258546
TITLE: [Micro-traumatic pathology of lumbar isthmus: Isthmic lysis or spondylolysis].

LA PATHOLOGIE MICRO-TRAUMATIQUE DES ISTHMES LOMBAIRES: LYSE ISTHMIQUE OU SPONDYLOLYSE.

AUTHOR: Drevet J.G.; Auberge T.; Magnol A.; Lelong C.; Blanc D.; Ramponneau J.P.

CORPORATE SOURCE: Centre Clinique Rhumatologique, 4, Boulevard Marechal Foch, F 38000 Grenoble, France

SOURCE: Revue du Rhumatisme et des Maladies Osteo-Articulaires, (1990) 57/5 (385-392).
ISSN: 0035-2659 CODEN: RRMOA2

COUNTRY: France

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 031 Arthritis and Rheumatism

LANGUAGE: French

SUMMARY LANGUAGE: English

AB The authors report the study of a series of 23 partial isthmic lyses which occurred in a young population (15 cases) and in an adult one (8 cases) between 1983 and 1988, in the form of persistent lumbosacral pains. The initial radiological signs, the key to an early diagnosis, are defined: cortical **notches** more often regarding the lower cortex than the upper one, incomplete fissures reaching the two cortical poles, gradual narrowing of the isthmus. The value of standard radiography is underlined, with the oblique incidences close to the profile regularly ensuring the diagnosis, with the exception of 4 cases out of 23 for which tomography was required. As regards the evolution, the value of the diagnosis of the initial lesions is recalled, giving the hope of a restoration of the posterior inter-articular fractures by a rigid setting (4 months on average). This ability to reconstruct the lumbar isthmus is observed in the young subjects (10 out of 13 immobilizations) but also in the adult subjects (3 reconstructions for 5 immobilizations carried out). These results enable the early detection of prelytic states, in order to **administer** an suitable treatment resting on the rigid setting of the lumbosacral region, re-education and the control of the risk factors.

SO Revue du Rhumatisme et des Maladies Osteo-Articulaires, (1990) 57/5 (385-392).
ISSN: 0035-2659 CODEN: RRMOA2

AB . . . in the form of persistent lumbosacral pains. The initial radiological signs, the key to an early diagnosis, are defined: cortical **notches** more often regarding the lower cortex than the upper one, incomplete fissures reaching the two cortical poles, gradual narrowing of. . . subjects (3 reconstructions for 5 immobilizations carried out). These results enable the early detection of prelytic states, in order to **administer** an suitable treatment resting on the rigid setting of the lumbosacral region, re-education and the control of the risk factors.

L15 ANSWER 56 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 90084457 EMBASE

DOCUMENT NUMBER: 1990084457

TITLE: Cellular electrophysiological effects of flecainide on human atrial fibres.

AUTHOR: Le Grand B.; Le Heuzey J.-Y.; Perier P.; Peronneau P.; Lavergne T.; Hatem S.; Guize L.

CORPORATE SOURCE: U 256 INSERM, Instrum./Dynam. Cardiovascul., Hopital Broussais, 96 rue Didot,75674 Paris Cedex 14, France

SOURCE: Cardiovascular Research, (1990) 24/3 (232-238).
ISSN: 0008-6363 CODEN: CVREAU

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
027 Biophysics, Bioengineering and Medical Instrumentation
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Study objective - The aim of the study was to examine the electrophysiological characteristics of human atrial specimens collected during heart surgery and to investigate the effects of the class I antiarrhythmic agent flecainide on their electrical activity. Design - Atrial specimens were studied using standard microelectrode techniques, with and without superfused flecainide (5 x 10-7 M) or the transient outward current inhibitor 4-aminopyridine (0.5 mM). Experimental material - Atrial fragments 0.5-1.0 cm2 were obtained at operation from 34 patients, mean age 30 years. There was no history of previous atrial arrhythmia in any patient and drug therapy was stopped 24 h before surgery. Measurements and main results - Two types of transmembrane action potential were identified: (1) triangular shaped potentials (group A, classically found in animal models); (2) potentials with a large plateau preceded by a **notch** (group B). The effect of flecainide was compared on the two types of action potential. In both, flecainide lessened the depolarisation rate. In group B, but not in group A, it increased the action potential duration at 50% and 90% repolarisation (APD50, APD90) and the effective refractory period. The **notch** in group B action potentials is generated by transient outward currents (I(to)). Inhibition of these currents, either by increasing the pacing rate or by adding 4-aminopyridine, limited the increase in APD5'0, APD90, and effective refractoy period generated by the presence of flecainide. Conclusions - The effects of flecainide on the atrial repolarisation process depend on the shape of the action potential. These effects are more marked in cells with a plateau, where I(to) is activated.

SO Cardiovascular Research, (1990) 24/3 (232-238).
ISSN: 0008-6363 CODEN: CVREAU

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CT Medical Descriptors:
*action potential
*heart contraction
*heart electrophysiology
human cell
human
topical drug administration
article
priority journal
*4 aminopyridine: DO, drug dose
*4 aminopyridine: CM, drug comparison
*flecainide: DO, drug dose
*flecainide: CM, drug comparison

L15 ANSWER 57 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 89286148 EMBASE
DOCUMENT NUMBER: 1989286148
TITLE: In utero cleft lip repair in the mouse without an incision.
AUTHOR: Sullivan W.G.
CORPORATE SOURCE: Center for Fetal Diagnosis and Therapy, Wayne State University School of Medicine, Detroit, MI 48201, United States
SOURCE: Plastic and Reconstructive Surgery, (1989) 84/5 (723-730).
ISSN: 0032-1052 CODEN: PRSUAS
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 010 Obstetrics and Gynecology
034 Plastic Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In utero cleft lip repairs were done by full-thickness approximation of the cleft edges by 11-0 sutures in the A/J mouse on day 17 of gestation after Dilantin was **administered** on day 10. On day 20, a cesarean section was performed, the repair inspected, and the lip sectioned for histologic study. One-thousand one-hundred and thirty-nine mice were bred, and surgery was performed on 48. At least one fetus was present that had a cleft lip in 21 mice, and repairs were done on 16 fetuses. Ultimately, 9 viable fetuses were studied. In all cases, lip continuity was present where the suture had coapted the edges. There was little or no evidence of the lip repair despite no incision being performed. Histologic examination revealed epithelial and mesenchymal continuity with an occasional **notch** noted in the epithelium and soft-tissue asymmetry in complete clefts. The implications of these findings are discussed.
SO Plastic and Reconstructive Surgery, (1989) 84/5 (723-730).
ISSN: 0032-1052 CODEN: PRSUAS
AB . . . approximation of the cleft edges by 11-0 sutures in the A/J mouse on day 17 of gestation after Dilantin was **administered** on day 10. On day 20, a cesarean section was performed, the repair inspected, and the lip sectioned for histologic. . . evidence of the lip repair despite no incision being performed. Histologic examination revealed epithelial and mesenchymal continuity with an occasional **notch** noted in the epithelium and soft-tissue asymmetry in complete clefts. The implications of these findings are discussed.

L15 ANSWER 58 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 89186342 EMBASE
DOCUMENT NUMBER: 1989186342
TITLE: Value of intrauterine device insertion and estrogen **administration** after hysteroscopic metroplasty.
AUTHOR: Vercellini P.; Fedele L.; Arcaini L.; Rognoni M.T.; Candiani G.B.
CORPORATE SOURCE: First Department of Obstetrics and Gynecology, University of Milan, 20122 Milan, Italy
SOURCE: Journal of Reproductive Medicine for the Obstetrician and Gynecologist, (1989) 34/7 (447-450).
ISSN: 0024-7758 CODEN: JRPMAP
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 010 Obstetrics and Gynecology
014 Radiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Hysteroscopic metroplasty seems the treatment of choice for septate uterus. Little information is available on the possible usefulness of postoperative intrauterine device (IUD) insertion and estrogen **administration** in preventing fusion of a freshly cut septum and intrauterine adhesion formation. A hysterescopic incision in a uterine septum was made in 20 women. Postoperatively an IUD was inserted in ten of them and conjugated estrogens **administered** for 30 days with medroxyprogesterone accetate on days 26-30 (group I); the other ten were given no other therapeutic measures (group II). On follow-up hysterography five women in group I had a normal uterine cavity, and five had a residual fundal **notch** .gtoreq. 1 cm. In group II four had a normal uterine cavity, and six had a residual fundal **notch** .gtoreq. 1 cm. No intrauterine adhesions were detected in any of the patients. IUD insertion and hormonal therapy after hysteroscopic metroplasty do not seem to be needed to prevent septal fusion.
TI Value of intrauterine device insertion and estrogen **administration** after hysteroscopic metroplasty.
SO Journal of Reproductive Medicine for the Obstetrician and Gynecologist, (1989) 34/7 (447-450).
ISSN: 0024-7758 CODEN: JRPMAP
AB . . . choice for septate uterus. Little information is available on the possible usefulness of postoperative intrauterine device (IUD) insertion and estrogen **administration** in preventing fusion of a freshly cut septum and intrauterine adhesion formation. A hysterescopic incision in a uterine septum was made in 20 women. Postoperatively an IUD was inserted in ten of them and conjugated estrogens **administered** for 30 days with medroxyprogesterone accetate on days 26-30 (group I); the other ten were given no other therapeutic measures. . . II). On follow-up hysterography five women in group I had a normal uterine cavity, and five had a residual fundal **notch** .gtoreq. 1 cm. In group II four had a normal uterine cavity, and six had a residual fundal **notch** .gtoreq. 1 cm. No intrauterine adhesions were detected in any of the patients. IUD insertion and hormonal therapy after hysteroscopic. . .

L15 ANSWER 59 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 89073803 EMBASE
DOCUMENT NUMBER: 1989073803
TITLE: Multimodal treatment of hepatocellular carcinoma.
AUTHOR: Shimamura Y.; Takenaka Y.; Ishii M.; Shima Y.; Taniguchi H.; Kitai Y.; Watanabe H.; Sugai S.; Takahsi A.; Kitaya T.; Matsuyama T.; Hasegawa H.
CORPORATE SOURCE: Department of Surgery, National Matsudo Hospital, Chiba 271, Japan
SOURCE: Cancer Chemotherapy and Pharmacology, (1989) 23/SUPPL. (S87-S89).
ISSN: 0344-5704 CODEN: CCPHDZ
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 006 Internal Medicine
009 Surgery
016 Cancer
048 Gastroenterology
030 Pharmacology

037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Our multimodal treatment of hepatocellular carcinoma (HCC) has brought about a significant improvement of the survival rate. It consists of a combination of hepatectomy and transcatheter arterial embolization using lipiodol (L-TAE). In order to facilitate L-TAE, we have developed a special catheter with **notches**. A group of patients with HCC (124 cases), excluding cases with absolutely non-curative resections and operative deaths, were treated between December 1980 and November 1986. Each case was treated for more than 1 year after hepatectomy. The patients were divided into two groups: A, patients with a single tumor not larger than 5 cm, and B, cases with larger tumors or more than one lesion. Some patients in each group were treated with L-TAE after hepatectomy. In group A, there was no significant difference in survival between treated and non-treated cases. In group B, L-TAE gave a significantly better survival than no postoperative treatment.
SO Cancer Chemotherapy and Pharmacology, (1989) 23/SUPPL. (S87-S89).
ISSN: 0344-5704 CODEN: CCPHDZ
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CT Medical Descriptors:
*artificial embolism
*liver cancer: DT, drug therapy
*liver cancer: SU, surgery
survival
major clinical study
human
methodology
intraarterial drug administration
priority journal
iodinated poppyseed oil
*doxorubicin: DT, drug therapy
dibekacin

L15 ANSWER 60 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 88273763 EMBASE
DOCUMENT NUMBER: 1988273763
TITLE: Effect of doppler echocardiography to determine the cardiac effects of dobutamine in volunteers.
AUTHOR: Harry J.D.; Millson D.S.; Morton P.B.
CORPORATE SOURCE: Clinical Pharmacology Unit, ICI Pharmaceuticals, Macclesfield, United Kingdom
SOURCE: Pharmaceutical Medicine, (1988) 3/2-3 (173-183).
ISSN: 0265-0673 CODEN: PHMDEH
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We have assessed the ability of doppler echocardiography, both continuous and pulsed wave, to measure changes in cardiac function in human volunteers following dobutamine infusions. Changes in peak velocity and stroke distance were measured in the ascending aorta by angulating a 2 mHz (Vingmed) carrier probe in the suprasternal **notch** and analysing velocity time profile using a Doptek Spectrascan. Fifty pairs of measurements were analysed for continuous and pulsed wave doppler in six volunteers, who received two separate dobutamine infusions (1, 2, 4 .mu.g per kg per min i.v.) separated by one week. Significant dose-dependent increases in systolic blood pressure, peak velocity (PV) and stroke distance (SD) were observed with dobutamine when compared with normal saline infusions. Pulsed and continuous wave measurements were significantly correlated ($P < 0.001$). No significant differences were detected between mean systolic blood pressure, stroke distance and peak velocity measured on week 1 or week 2. Mean day to day coefficients of variation giving within subject repeatability (with range) were, for pulsed wave PV 2.5% (2.1-4.8), SD 8.3% (4.8-9.9), and for continuous wave PV 6.9% (4.6-14.7%), SD 6.6% (4.3-13.7). Variability between paired measurements separated by one week for peak velocity was 6.5% (pulsed wave) and 10.8% (continuous wave) and similarly 13.3% and 10.7% for stroke distance measurements. Doppler echocardiography can non-invasively estimate drug induced inotropic changes in healthy volunteers. Dobutamine-induced increases in peak velocity in excess of 14% and stroke distance of greater than 22% can be detected with a probability greater than 0.95 using pulsed doppler.
SO Pharmaceutical Medicine, (1988) 3/2-3 (173-183).
ISSN: 0265-0673 CODEN: PHMDEH
AB . . . and stroke distance were measured in the ascending aorta by angulating a 2 mHz (Vingmed) carrier probe in the suprasternal **notch** and analysing velocity time profile using a Doptek Spectrascan. Fifty pairs of measurements were analysed for continuous and pulsed wave. . .
CT Medical Descriptors:
*doppler echocardiography
*heart function
blood pressure
heart rate
volunteer
normal human
human experiment
human
methodology
male
intravenous drug administration
*dobutamine: PD, pharmacology
*dobutamine: DO, drug dose

L15 ANSWER 61 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 88181544 EMBASE
DOCUMENT NUMBER: 1988181544
TITLE: IV contrast material for abdominal CT: Comparison of three methods of **administration**.
AUTHOR: Platt J.F.; Glazer G.M.
CORPORATE SOURCE: Department of Radiology, University of Michigan Medical Center, Ann Arbor, MI 48109-0030, United States
SOURCE: American Journal of Roentgenology, (1988) 151/2 (275-277).

ISSN: 0361-803X CODEN: AJROAM
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 014 Radiology
028 Urology and Nephrology
048 Gastroenterology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Despite a decade of experience, there is still no consensus as to the optimal IV contrast regimen for use in combined abdominal and pelvic CT scanning. In order to determine which regimen is most effective, 90 patients undergoing CT were prospectively randomized into one of three groups, depending on the method by which IV contrast material was **administered**: (1) a single bolus (150 ml or 175 ml, depending on the patient's weight) started when scans were made at the level of the dome of the diaphragm; (2) a split bolus delivered by means of a power injector, with the first bolus (100 or 125 ml) given when scans were made at the level of the dome of the diaphragm and the second bolus (50 ml) given when scans were made at the level of the iliac crest; (3) an initial hand-delivered bolus (100 or 125 ml) given when scans were made at the level of diaphragm, followed by rapid IV drip infusion of 50 ml throughout the remainder of the study. Quantitative comparison of pre- and postcontrast scans was performed at two levels: at the mid-liver to assess hepatic enhancement and 1 cm above the sacrosciatic **notch** to assess pelvic vascular enhancement. The single bolus provided better mean liver enhancement (46 H) than did either the split-bolus (36 H) or the bolus-drip (32 H) method ($p < .05$). The last two methods achieved a sufficient aortacaval difference (>10 H) to allow for evaluation of the liver in the nonequilibrium phase of contrast enhancement in which lesion detection is thought to be optimal. Mean enhancement of pelvic vessels was significantly better with the split bolus (arterial enhancement of 56 H, venous enhancement of 47 H) than with the single bolus (34 H, 31 H) or bolus-drip infusion (38 H, 35 H) ($p < .05$). We conclude that the split-bolus method is optimal for routine combined abdominal and pelvic CT scanning. The bolus-drip method is the least effective method for **administering** the contrast material.

TI IV contrast material for abdominal CT: Comparison of three methods of **administration**.

SO American Journal of Roentgenology, (**1988**) 151/2 (275-277).
ISSN: 0361-803X CODEN: AJROAM

AB . . . undergoing CT were prospectively randomized into one of three groups, depending on the method by which IV contrast material was **administered**: (1) a single bolus (150 ml or 175 ml, depending on the patient's weight) started when scans were made at. . . postcontrast scans was performed at two levels: at the mid-liver to assess hepatic enhancement and 1 cm above the sacrosciatic **notch** to assess pelvic vascular enhancement. The single bolus provided better mean liver enhancement (46 H) than did either the split-bolus. . . method is optimal for routine combined abdominal and pelvic CT scanning. The bolus-drip method is the least effective method for **administering** the contrast material.

CT Medical Descriptors:
*abdomen
*computer assisted tomography
*contrast enhancement
comparative study
computer analysis
major clinical study
human
methodology
economic aspect
intravenous drug administration
*meglumine diatrizoate: DT, drug therapy
***meglumine diatrizoate: AD, drug administration**

L15 ANSWER 62 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 88116367 EMBASE
DOCUMENT NUMBER: 1988116367
TITLE: Use of exercise Doppler echocardiography to evaluate cardiac drugs: Effects of propranolol and verapamil on aortic blood flow velocity and acceleration.
AUTHOR: Harrison M.R.; Smith M.D.; Nissen S.E.; Grayburn P.A.; DeMaria A.N.
CORPORATE SOURCE: Division of Cardiology, University of Kentucky Medical Center, Lexington, KY 40536, United States
SOURCE: Journal of the American College of Cardiology, (**1988**) 11/5 (1002-1009).
ISSN: 0735-1097 CODEN: JACCDI
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB This study evaluated the ability of exercise Doppler echocardiography to identify hemodynamic changes due to cardiac medication. Twenty young healthy volunteers (mean age 30 years) underwent continuous wave Doppler examination from the suprasternal **notch** at rest, during each stage of a standard exercise protocol and immediately after exercise. On completion of the control test, each subject received either 60 to 80 mg of propranolol or 120 mg of verapamil orally, and the same exercise protocol was repeated after 90 min. During the control test, values for modal velocity, acceleration and flow velocity integral all increased significantly from baseline ($p < 0.0002$ for each). When exercise was repeated after propranolol **administration**, values for all Doppler measurements were significantly altered. Modal velocity at baseline was significantly lower after propranolol when compared with control (0.53 .+-. 0.11 versus 0.63 .+-. 0.17 m/s; $p < 0.0001$). Similarly, modal velocity at maximal exercise was significantly lower after propranolol (1.11 .+-. 0.2 versus 1.25 .+-. 0.21 m/s; $p < 0.0001$). The effect of propranolol on acceleration was even greater, with blunting of baseline (11.4 .+-. 2 versus 15.4 .+-. 5 m/s per s; $p < 0.0005$) and exertional (33.4 .+-. 10 versus 56.3 .+-. 15 m/s; $p < 0.0001$) acceleration. The flow velocity integral during exercise was greater after propranolol (14.1 .+-. 3.1 versus 10.1 .+-. 3.2 cm; $p < 0.0005$) than during the control test. Verapamil failed to influence any Doppler-measured index of aortic blood flow. It is concluded that: 1) propranolol exerts a profound hemodynamic effect as measured by Doppler echocardiography at rest and during exercise; 2) despite its negative inotropic properties, propranolol results in an increased stroke volume

during exercise, apparently because of increased preload; 3) verapamil, in the dosages studied, does not alter the Doppler-measured exercise response in young healthy subjects; and 4) Doppler echocardiography is a useful technique for evaluating the hemodynamic effects of medication on aortic blood flow at rest and during exercise.

SO Journal of the American College of Cardiology, (1988) 11/5 (1002-1009).
ISSN: 0735-1097 CODEN: JACCDI

AB . . . due to cardiac medication. Twenty young healthy volunteers (mean age 30 years) underwent continuous wave Doppler examination from the suprasternal **notch** at rest, during each stage of a standard exercise protocol and immediately after exercise. On completion of the control test,. . . and flow velocity integral all increased significantly from baseline ($p < 0.0002$ for each). When exercise was repeated after propranolol **administration**, values for all Doppler measurements were significantly altered. Modal velocity at baseline was significantly lower after propranolol when compared with. . .

CT Medical Descriptors:
*aorta
*blood flow velocity
*doppler echocardiography
adult
exercise
priority journal
human
controlled study
human experiment
male
female
oral drug administration
drug therapy
*propranolol: PD, pharmacology
*propranolol: CM, drug comparison
*propranolol: CT, clinical trial
*verapamil: PD, pharmacology
*verapamil: CM, drug comparison
*verapamil: CT, clinical trial

L15 ANSWER 63 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 88078262 EMBASE
DOCUMENT NUMBER: 1988078262
TITLE: Effects of tracheal intubation on laryngeal acoustic waveforms.
AUTHOR: Priebe H.-J.; Henke W.; Hedley-Whyte J.
CORPORATE SOURCE: Department of Anesthesia, University Hospital, Basel, Switzerland
SOURCE: Anesthesia and Analgesia, (1988) 67/3 (219-227).
ISSN: 0003-2999 CODEN: AACRAT
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 024 Anesthesiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB To assess the feasibility of noninvasive detection of laryngeal injury after tracheal intubation through acoustic waveform measurements, we studied the effects of intubation on 'time-expanded' acoustic waveforms of the larynx in 16 patients given general anesthesia, 9 with and 7 without tracheal intubation. Recordings of several utterances were obtained by means of a microphone and an accelerometer attached to the skin at the midpoint of the suprasternal **notch**. Recordings were taken the day before induction of general anesthesia, 20 minutes after extubation, and 2 and 4 days after extubation. Waveforms of the recordings were subsequently assessed visually for features different from those of normal phonation as determined in preliminary studies. Waveforms in several of the recordings taken soon after extubation showed marked intraperiod and interperiod irregularities. These abnormalities improved and disappeared over the following 4 days. No changes were observed in the acoustic waveforms of seven patients given general anesthesia without tracheal intubation. The analysis of time-expanded acoustic waveforms of the larynx indicates that this technique has considerable potential as a sensitive, noninvasive technique that helps to evaluate the effects of tracheal intubation on laryngeal function, a technique that warrants further study and evaluation.

SO Anesthesia and Analgesia, (1988) 67/3 (219-227).
ISSN: 0003-2999 CODEN: AACRAT

AB . . . were obtained by means of a microphone and an accelerometer attached to the skin at the midpoint of the suprasternal **notch**. Recordings were taken the day before induction of general anesthesia, 20 minutes after extubation, and 2 and 4 days after. . .

CT Medical Descriptors:
*accelerometer
*general anesthesia
*intubation
adult
larynx
larynx injury: SI, side effect
clinical article
human
inhalational drug administration

L15 ANSWER 64 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 88043735 EMBASE
DOCUMENT NUMBER: 1988043735
TITLE: Putative stimulants for functional recovery after neural trauma: Only spermine was effective.
AUTHOR: Kauppila T.; Stenberg D.; Porkka-Heiskanen T.
CORPORATE SOURCE: Department of Physiology, University of Helsinki, 00170 Helsinki, Finland
SOURCE: Experimental Neurology, (1988) 99/1 (50-58).
ISSN: 0014-4886 CODEN: EXNEAC
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 002 Physiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The motor functional recovery after sciatic nerve crush was measured in rats treated with daily injections of (a) thyrotropin-releasing hormone (2.0 mg/kg), (b) alpha-melanocyte-stimulating hormone (0.07 mg/kg/48 h), or (c) testosterone propionate (4.4 mg/kg). The recovery of the motor function of the sciatic nerve was indicated by using the return of the

toe-spreading response. None of the treatments differed significantly from saline controls in the time needed for recovery. The same procedure (without injections) was carried out with castrated and noncastrated male rats in order to test the effect of the lack of testosterone on recovery time after sciatic crush. The groups did not differ significantly as to their recovery times. The same method was used to study the effect of spermine (10.0 mg/kg/day) on the recovery of motor function. Spermine seemed to reduce the time needed for recovery from a mean value of 15.7 to 11.0 days ($P < 0.01$). We also studied the effect of daily injections of spermine (13.0 mg/kg) on the sensory division of the peripheral nerve using the foot-flick test. The time needed for recovery after crush in the sciatic **notch** was reduced from 13.7 to 7.7 days ($P < 0.005$). These results do not support the hypothesis that alpha-melanocyte-stimulating hormone, thyrotropin-releasing hormone, or testosterone enhance functional recovery of severed motor axons. Our results confirm a previous observation that spermine reduces the time needed for recovery after trauma in peripheral motor neurons. The result of the foot-flick test suggests that spermine enhances both motor and sensory recovery.

SO Experimental Neurology, (**1988**) 99/1 (50-58).
ISSN: 0014-4886 CODEN: EXNEAC

AB . . . sensory division of the peripheral nerve using the foot-flick test. The time needed for recovery after crush in the sciatic **notch** was reduced from 13.7 to 7.7 days ($P < 0.005$). These results do not support the hypothesis that alpha-melanocyte-stimulating hormone,. . .

CT Medical Descriptors:
*motor performance
*nerve injury: DT, drug therapy
*prognosis
*sciatic nerve
*therapy
rat
animal experiment
nonhuman
intraperitoneal drug administration
subcutaneous drug administration
*alpha intermedin
*protirelin
*spermine
*testosterone propionate

L15 ANSWER 65 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 87173902 EMBASE
DOCUMENT NUMBER: 1987173902
TITLE: An inward calcium current underlying regenerative calcium potentials in rat striatal neurons in vitro enhanced by BAY K 8644.
AUTHOR: Cherubini E.; Lanfumey L.
CORPORATE SOURCE: INSERM U.029, 75014 Paris, France
SOURCE: Neuroscience, (**1987**) 21/3 (997-1005).
CODEN: NRSCDN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
002 Physiology
LANGUAGE: English

AB The single electrode voltage clamp technique was used to characterize the currents underlying the calcium potentials in rat caudate neurons in vitro. In current clamp experiments, long depolarizing current pulses evoked repetitive firing of fast somatic action potentials. These were preceded by a transient hyperpolarizing **notch**. Addition of 4-aminopyridine (100 .mu.M) abolished the hyperpolarizing **notch**, enhanced the slow graded depolarizing response and induced the appearance of a slow all-or-nothing action potential. Both the slow graded response and the all-or-nothing action potential were abolished by cobalt (2 mM), suggesting the involvement of voltage-dependent calcium conductances. When the neurons were loaded intracellularly with caesium the action potential duration increased. Substitution of the extracellular calcium by barium (1-3 mM) or external addition of tetraethylammonium (5 mM) further prolonged spike duration and induced the appearance of long-lasting plateau potentials. These were insensitive to tetrodotoxin and were reversibly blocked by the calcium antagonists cobalt (2 mM), manganese (2 mM) or cadmium (500 .mu.M). The calcium potentials were enhanced by the calcium 'agonist' BAY K 8644 (1-5 .mu.M). In voltage clamp experiments when intracellular caesium was used to reduce outward currents and tetrodotoxin to block fast regenerative sodium currents, depolarizing voltage steps from a holding potential of -50, -40 mV activated an inward current. This current peaked in 50-80 ms and inactivated in two phases: an initial one at 150-200 ms followed by a second one after several hundred ms. The current was still inward at the end of the command step and often was followed by an inward tail current. The current/voltage curve was N-shaped with a region of negative slope conductance between -25 and -10 mV. The inward current was larger in the presence of barium (1-3 mM) and tetraethylammonium (5 mM). It was abolished by the calcium antagonists cobalt (2 mM) and cadmium (500 .mu.M) and enhanced by the calcium 'agonist' BAY K 8644 (5 .mu.M). In conclusion, like many other central neurons, striatal neurons bear calcium conductances that underlie the calcium potentials observed in current clamp experiments.

SO Neuroscience, (**1987**) 21/3 (997-1005).
CODEN: NRSCDN

AB . . . experiments, long depolarizing current pulses evoked repetitive firing of fast somatic action potentials. These were preceded by a transient hyperpolarizing **notch**. Addition of 4-aminopyridine (100 .mu.M) abolished the hyperpolarizing **notch**, enhanced the slow graded depolarizing response and induced the appearance of a slow all-or-nothing action potential. Both the slow graded. . .

CT Medical Descriptors:
*calcium conductance
*calcium current
*caudate nucleus
*corpus striatum
*dose response
*drug antagonism
*drug comparison
*drug efficacy
*drug mechanism
*electric potential
*nerve cell
rat
priority journal
pharmacokinetics
drug administration
animal cell

methodology
etiology
animal
central nervous system
nervous system
*1,4 dihydro 2,6 dimethyl 5 nitro 4 [2 (trifluoromethyl)phenyl] 3 pyridinecarboxylic acid methyl ester
*tetrodotoxin
barium chloride
cadmium. . .

L15 ANSWER 66 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 87173173 EMBASE
DOCUMENT NUMBER: 1987173173
TITLE: Prolonged increase in digital blood flow following iloprost infusion in patients with systemic sclerosis.
AUTHOR: Rademaker M.; Thomas R.H.M.; Provost G.; et al.
CORPORATE SOURCE: Department of Dermatology, St Bartholomew's Hospital, London EC1A 7BE, United Kingdom
SOURCE: Postgraduate Medical Journal, (1987) 63/742 (617-620).
CODEN: PGMJAO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English
AB Thirteen patients with Raynaud's phenomenon secondary to systemic sclerosis received three 8-hour infusions of a synthetic prostacyclin analogue (Iloprost) on consecutive days and were followed-up over a period of 10 weeks during the winter of 1985/86. Six weeks after infusion, digital peripheral vascular resistance had fallen ($P < 0.05$) and dicrotic **notch** proportion of pulse amplitude increased ($P < 0.05$). Digital blood flow and pulse amplitude (measured by photoplethymography) were also increased but did not reach statistical significance. The trend of improvement in these blood flow parameters was still evident after 10 weeks. The number of cutaneous lesions (digital ulcers, etc) fell from 26 lesions before infusion to only 7 lesions by the end of the study, confirming the subjective improvement reported by the patients.
SO Postgraduate Medical Journal, (1987) 63/742 (617-620).
CODEN: PGMJAO
AB . . . during the winter of 1985/86. Six weeks after infusion, digital peripheral vascular resistance had fallen ($P < 0.05$) and dicrotic **notch** proportion of pulse amplitude increased ($P < 0.05$). Digital blood flow and pulse amplitude (measured by photoplethymography) were also increased. . .
CT Medical Descriptors:
*blood flow
*drug efficacy
*raynaud phenomenon
*systemic sclerosis
peripheral vascular system
priority journal
intravenous drug administration
human
diagnosis
therapy
clinical article
*iloprost
*prostacyclin

L15 ANSWER 67 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 87086143 EMBASE
DOCUMENT NUMBER: 1987086143
TITLE: Influence of sublingual nitroglycerin on the digital circulation of man.
AUTHOR: Burch G.E.
CORPORATE SOURCE: Department of Medicine, Tulane School of Medicine, New Orleans, LA 70112, United States
SOURCE: Angiology, (1986) 37/11 (801-809).
CODEN: ANGIAB
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English
AB By means of the digital rheoplethysmographic (RPG) method, the effect of sublingually **administered** nitroglycerin (NTG), 1/200 gr (0.3 mg), on the digital circulation was studied in 17 normal subjects and 5 patients with ischemic heart disease and angina pectoris. NTG produced dilatation of all digital vessels, reflected especially by increases in total digital volume. NTG produced marked changes in the dicrotic **notch** of the pulse wave, noted also in inflow volume curves but not in outflow volume curves. The dichrotic **notch** was displaced later on the descending limb of the digital pulse wave and became deeper and more prominent after NTG. It is suggested that NTG produces disproportionate dilatation of the arterial system, having its greatest effect on arteries near the heart, including the coronaries and great vessels branching off the aorta, and on left intraventricular cavity pressure. This greater regional vasodilatation of vessels near the heart could delay closure of the aortic valve, producing a delayed and prominent dicrotic **notch** of the pulse wave.
SO Angiology, (1986) 37/11 (801-809).
CODEN: ANGIAB
AB By means of the digital rheoplethysmographic (RPG) method, the effect of sublingually **administered** nitroglycerin (NTG), 1/200 gr (0.3 mg), on the digital circulation was studied in 17 normal subjects and 5 patients with. . . dilatation of all digital vessels, reflected especially by increases in total digital volume. NTG produced marked changes in the dicrotic **notch** of the pulse wave, noted also in inflow volume curves but not in outflow volume curves. The dichrotic **notch** was displaced later on the descending limb of the digital pulse wave and became deeper and more prominent after NTG. . . . regional vasodilatation of vessels near the heart could delay closure of the aortic valve, producing a delayed and prominent dicrotic **notch** of the pulse wave.
CT Medical Descriptors:
*angina pectoris
*drug efficacy
*ischemic heart disease
*drug therapy
finger circulation

heart
priority journal
therapy
sublingual drug administration
human
cardiovascular system
peripheral vascular system
clinical article
*glyceryl trinitrate

L15 ANSWER 68 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 86044246 EMBASE
DOCUMENT NUMBER: 1986044246
TITLE: [Drug-induced ulcers in endoscopic lesions of the oesophagus].
IMPORTANCE DES ULCERATIONS MEDICAMENTEUSES DANS LES LESIONS ENDOSCOPIQUES DE L'OESOPHAGE.
AUTHOR: Baeriswyl G.; Bengoa J.; De Peyer R.; Loizeau E.
CORPORATE SOURCE: Division de Gastro-Enterologie et Nutrition, Hopital Cantonal Universitaire, CH-1211 Geneve 4, Switzerland
SOURCE: Schweizerische Medizinische Wochenschrift, (1985) SUPPL. 19/- (6-9).
CODEN: SMWOAS
COUNTRY: Switzerland
DOCUMENT TYPE: Journal
FILE SEGMENT: 038 Adverse Reactions Titles
037 Drug Literature Index
006 Internal Medicine
048 Gastroenterology
030 Pharmacology
LANGUAGE: French
SUMMARY LANGUAGE: English
AB Drug-induced ulcers of the oesophagus represent a rare but probably under-recorded complication. In a series of 5900 endoscopies performed in 32 months, oesophageal ulcers were seen in 4 cases following the intake of doxycycline, and in one case after ingestion of pinaverium bromide and a bulk laxative respectively. Oesophageal ulcers were seen mainly in young patients without underlying oesophageal disease, presenting with chest pain and odynophagia. The most common site of involvement was at the aortic **notch** in the middle third of the oesophagus. The course was quickly favorable within 5-10 days after the drug was discontinued, but transient complete abstention from oral intake was required in some cases. Ulceration is thought to be secondary to drug stasis and local cytotoxic effects. Oesophageal ulcers can be prevented simply by recommending intake of the drug with sufficient water in the upright position at least two hours before retiring.
SO Schweizerische Medizinische Wochenschrift, (1985) SUPPL. 19/- (6-9).
CODEN: SMWOAS
AB . . . without underlying oesophageal disease, presenting with chest pain and odynophagia. The most common site of involvement was at the aortic **notch** in the middle third of the oesophagus. The course was quickly favorable within 5-10 days after the drug was discontinued,. . .
CT Medical Descriptors:
*adverse drug reaction
*agiolax
*cytotoxicity
*endoscopy
*esophagitis
*esophagus ulcer
*gastrointestinal toxicity
*drug therapy
esophagus
therapy
intoxication
oral drug administration
human
diagnosis
clinical article
*antibiotic agent
*antiinflammatory agent
*clindamycin
*cotrimoxazole
*doxycycline
*doxycycline hyclate
*emepronium bromide
*fluorouracil
*indometacin
*laxative
*penicillin v
*pinaverium bromide
*potassium chloride
*prednisolone
*quinidine
tetracycline
agiolax
unclassified drug

L15 ANSWER 69 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 84080219 EMBASE
DOCUMENT NUMBER: 1984080219
TITLE: Effect of tubocurarine on static and dynamic muscle contractions in man.
AUTHOR: Secher N.H.; Petersen S.; Grimby G.
CORPORATE SOURCE: Department P, Bispebjerg Hospital, Copenhagen, Denmark
SOURCE: Acta Physiologica Scandinavica, (1984) 120/2 (251-255).
CODEN: APSCAX
COUNTRY: Sweden
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
002 Physiology
019 Rehabilitation and Physical Medicine
008 Neurology and Neurosurgery
030 Pharmacology
LANGUAGE: English
AB The effect of bolus injection of tubocurarine (0.1 mg x kg-1 i.v.) was followed in six young subjects by registration of static, and slow (30.degree. x s-1) and fast (150.degree. x s-1) dynamic (isokinetic) maximal voluntary leg extensions. Mechanograms from both unblocked and curarized muscle contractions showed a '**notch**' after about 440 ms separating two relative maxima. The mechanograms were divided by an

arbitrary straight line connecting the starting point of the contraction curve and the **notch**. The line separated an area (Nm x s) above and to the left (.alpha.-component) from an area below and to the right (.beta.-component) of the line. Tubocurarine affected the .beta.-component selectively until about 70% reduced in the static contractions. With further curarization and the .alpha.-component was also reduced in size. The .alpha.-component was equally affected during the three types of contractions, while the faster the contraction the more the .beta.-component was reduced. The results suggest that static as well as dynamic human muscle contractions can be divided into two parts with a different sensitivity for tubocurarine, one of which seems to have a sensitivity which depends on the contraction velocity.

SO Acta Physiologica Scandinavica, (**1984**) 120/2 (251-255).
CODEN: APSCAX

AB . . . fast (150.degree. x s-1) dynamic (isokinetic) maximal voluntary leg extensions. Mechanograms from both unblocked and curarized muscle contractions showed a '**notch**' after about 440 ms separating two relative maxima. The mechanograms were divided by an arbitrary straight line connecting the starting point of the contraction curve and the **notch**. The line separated an area (Nm x s) above and to the left (.alpha.-component) from an area below and to. . .

CT Medical Descriptors:
*drug efficacy
*drug mechanism
*drug sensitivity
*dynamic muscle contraction
*muscle
*neuromuscular blocking
*static muscle contraction
intravenous drug administration
methodology
human
therapy
human experiment
peripheral nervous system
*tubocurarine chloride

L15 ANSWER 70 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 84035781 EMBASE
DOCUMENT NUMBER: 1984035781
TITLE: Soft-tissue injury caused by antineoplastic drugs is inhibited by topical dimethyl sulphoxide and alpha tocopherol.
AUTHOR: Nobbs P.; Barr R.D.
CORPORATE SOURCE: Department of Pediatrics, McMaster University, Hamilton, Ont., Canada
SOURCE: British Journal of Cancer, (**1983**) 48/6 (873-876).
CODEN: BJCAAI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 038 Adverse Reactions Titles
037 Drug Literature Index
016 Cancer
013 Dermatology and Venereology
030 Pharmacology
LANGUAGE: English

AB The present study was undertaken to examine the roles of DMSO and Vitamin E in the secondary prevention of soft tissue injury following the i.d. and s.c. injection of Adriamycin in Hartley guinea pigs which were obtained from Camm Research Institute Inc., Wayne, New Jersey and accomodated in groups of 3 or 4 per cage, receiving Purina Guinea Pig Chow and water ad libitum. Individual animals were identified by appropriate ear **notches**. The skin of the back was shaved and used as the target site. Shaving was repeated at intervals of one week.

SO British Journal of Cancer, (**1983**) 48/6 (873-876).
CODEN: BJCAAI

AB . . . or 4 per cage, receiving Purina Guinea Pig Chow and water ad libitum. Individual animals were identified by appropriate ear **notches**. The skin of the back was shaved and used as the target site. Shaving was repeated at intervals of one. . .

CT Medical Descriptors:
*adverse drug reaction
*drug extravasation
*skin necrosis
*skin toxicity
*soft tissue injury
extravasation
guinea pig
soft tissue
intoxication
subcutaneous drug administration
animal experiment
prevention
nonhuman
subcutaneous tissue
*alpha tocopherol
*antineoplastic agent
*dimethyl sulfoxide
*doxorubicin

L15 ANSWER 71 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 83103071 EMBASE
DOCUMENT NUMBER: 1983103071
TITLE: [Uterine anomalies in young women exposed to diethylstilbestrol in utero. Hysterographic findings in three cases].
ANOMALIES HYSTEROGRAPHIQUES CHEZ DE JEUNES FEMMES EXPOSEES IN UTERO AU DIETHYLSTILBESTROL. ETUDE PRELIMINAIRE A PROPOS DE 3 CAS.
AUTHOR: Caby J.
CORPORATE SOURCE: Serv. Endocrinol. Pathol. Reprod., Hop. Necker, F 75015 Paris, France
SOURCE: Gynecologie, (**1982**) 33/6 (515-521).
CODEN: GYNCAZ
COUNTRY: France
DOCUMENT TYPE: Journal
FILE SEGMENT: 038 Adverse Reactions Titles
010 Obstetrics and Gynecology
052 Toxicology
007 Pediatrics and Pediatric Surgery
037 Drug Literature Index
003 Endocrinology
014 Radiology

LANGUAGE: French
SUMMARY LANGUAGE: English
AB Uterine anomalies were found on hysterographic examination in 3 young women exposed to Distilbene in utero. A review of the published literature demonstrated that more than 2 out of 3 women exposed to Distilbene in utero presented anomalies on hysterography images: the uterus was usually hypoplasic in the form of a 'T', with **notches**, border spicules, and a characteristic appearance of body and/or horn strictures. These findings strongly suggest the need for hysterosalpingography in these patients, together with other investigational procedures, in order to detect these lesions, which have a significant adverse effect on future pregnancy possibilities.
SO Gynecologie, (**1982**) 33/6 (515-521).
CODEN: GYNCAZ
AB . . . Distilbene in utero presented anomalies on hysterography images: the uterus was usually hypoplasic in the form of a 'T', with **notches**, border spicules, and a characteristic appearance of body and/or horn strictures. These findings strongly suggest the need for hysterosalpingography in. . .
CT Medical Descriptors:
*adverse drug reaction
*chemical teratogenesis
*hysterography
*drug therapy
*prenatal drug exposure
*reproductive toxicity
*uterus malformation
pregnancy
female genital system
intoxication
therapy
drug administration
human
embryo
fetus
diagnosis
case report
*diethylstilbestrol

L15 ANSWER 72 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 83069032 EMBASE
DOCUMENT NUMBER: 1983069032
TITLE: Closed system enflurane in oxygen.
AUTHOR: Robins D.W.
CORPORATE SOURCE: Sir Humphry Davy Dep. Anaesth., R. Infirm., Bristol BS2 8HW, United Kingdom
SOURCE: Anaesthesia, (**1983**) 38/1 (56-60).
CODEN: ANASAB
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
024 Anesthesiology
LANGUAGE: English
AB A safe method of **administering** enflurane from a Goldman vaporizer in a closed system is described, using a fresh gas flow of 0.5 litres/minute of oxygen. There was a drawback, in that, until the system was closed, insufficient concentration of enflurane was achieved in seven out of 20 patients, who then moved on surgical incision. When the system was closed, the concentration of enflurane increased so that satisfactory anaesthesia occurred. The maximum inspired concentration of enflurane in the system was 4.5% which occurred in one patient on the 3rd **notch** of the Goldman. A portable interference refractometer was used to measure the percentage of enflurane.
SO Anaesthesia, (**1983**) 38/1 (56-60).
CODEN: ANASAB
AB A safe method of **administering** enflurane from a Goldman vaporizer in a closed system is described, using a fresh gas flow of 0.5 litres/minute of. . . occurred. The maximum inspired concentration of enflurane in the system was 4.5% which occurred in one patient on the 3rd **notch** of the Goldman. A portable interference refractometer was used to measure the percentage of enflurane.

L15 ANSWER 73 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 81098814 EMBASE
DOCUMENT NUMBER: 1981098814
TITLE: Superior gluteal artery haemorrhage following pelvic fractures controlled by embolisation.
AUTHOR: Sundaram M.; Patel B.; Wolverson M.K.; Riaz M.A.
CORPORATE SOURCE: Dept. Radiol., St Louis Univ. Hosp., St Louis, Mo. 63104, United States
SOURCE: Clinical Radiology, (**1981**) 32/2 (187-190).
CODEN: CLRAAG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 014 Radiology
033 Orthopedic Surgery
009 Surgery
037 Drug Literature Index
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English
AB Successful embolisation of active bleeding from the superior gluteal artery seen in two patients within the last 12 months is described. Both patients had extensive abdominal and pelvic injuries. One patient eventually died from renal failure and a perforated colon. The other patient is mobile and has been periodically seen in the out-patient department over the past nine months. In both instances, haemorrhage was at the sacrosciatic **notch**. Early angiography, in patients with extensive pelvic trauma and major blood requirements, with intent to embolise any identifiable bleeding source would appear to be the best initial manoeuvre to prevent exsanguination.
SO Clinical Radiology, (**1981**) 32/2 (187-190).
CODEN: CLRAAG
AB . . . been periodically seen in the out-patient department over the past nine months. In both instances, haemorrhage was at the sacrosciatic **notch**. Early angiography, in patients with extensive pelvic trauma and major blood requirements, with intent to embolise any identifiable bleeding source. . .
CT Medical Descriptors:
*artery bleeding
*artificial embolism
*bleeding
*pelvis fracture
*superior gluteal artery

angiography
drug therapy
bone
therapy
peripheral vascular system
case report
intraarterial drug administration
injury
pharmacokinetics
*gelfoam
contrast medium

L15 ANSWER 74 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 80146131 EMBASE
DOCUMENT NUMBER: 1980146131
TITLE: [Observations in phenprocoumon (Marcumar.RTM.) intoxication].
BEOBACHTUNGEN BEI PHENPROCOUMON-(MARCUMAR.RTM.-) VERGIFTUNG. ELIMINATION UND SERUMBINDUNG DES ANTIKOAGULANS BEI TOXISCHEN BLUTKONZENTRATIONEN.
AUTHOR: Held H.; Von Busse G.; Meissner J.
CORPORATE SOURCE: Inst. Exp. Biol. Med., 2061 Borstel, Germany
SOURCE: Deutsche Medizinische Wochenschrift, (1980) 105/24 (860-863).
CODEN: DMWOAX
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 038 Adverse Reactions Titles
037 Drug Literature Index
018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
LANGUAGE: German
SUMMARY LANGUAGE: English
AB Serial serum concentrations of phenprocoumon were measured in 2 female patients who had taken 150 and 450 mg of the drug in suicidal attempts. In one case absorption of phenprocoumon took nearly two days. At a concentration of 1.7 and 1.8 .mu.g/ml the elimination curve showed a **notch** in both patients. Above this concentration half life was 97.7 and 95.9 hours, below these levels 134.4 and 155.5 hours. In-vitro binding investigations with serum of a healthy proband showed an increase of the non-bound drug by 56.6% at a phenprocoumon concentration of 0.5-25.34 .mu.g/ml. As no **notch** could be observed at lower concentrations the **notch** in the elimination curve cannot be explained by concentration-dependent plasma binding of the anticoagulant. In-vitro experiments involving haemodialysis indicate that the latter cannot be recommended for treatment of phenprocoumon intoxication as the amount of phenprocoumon thus eliminated from the body is minimal. Both patients survived the phenprocoumon intoxication without damage. They were only treated with vitamin K.
SO Deutsche Medizinische Wochenschrift, (1980) 105/24 (860-863).
CODEN: DMWOAX
AB . . . absorption of phenprocoumon took nearly two days. At a concentration of 1.7 and 1.8 .mu.g/ml the elimination curve showed a **notch** in both patients. Above this concentration half life was 97.7 and 95.9 hours, below these levels 134.4 and 155.5 hours.. . . healthy proband showed an increase of the non-bound drug by 56.6% at a phenprocoumon concentration of 0.5-25.34 .mu.g/ml. As no **notch** could be observed at lower concentrations the **notch** in the elimination curve cannot be explained by concentration-dependent plasma binding of the anticoagulant. In-vitro experiments involving haemodialysis indicate that. . .
CT Medical Descriptors:
*adverse drug reaction
*drug blood level
*drug intoxication
*hemodialysis
*suicide attempt
oral drug administration
case report
pharmacokinetics
intoxication
*anticoagulant agent
*phenprocoumon
*menadione
phytomenadione

L15 ANSWER 75 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 80063313 EMBASE
DOCUMENT NUMBER: 1980063313
TITLE: Metrizamide lumbar epidurography with Seldinger technique through the sacral **notch** and selective nerve root injection.
AUTHOR: Hatten Jr. H.P.
CORPORATE SOURCE: Dept. Radiol., Presbyt. Hosp., Charlotte, N.C., United States
SOURCE: Neuroradiology, (1980) 19/1 (19-25).
CODEN: NRDYAB
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
014 Radiology
008 Neurology and Neurosurgery
LANGUAGE: English
AB Lumbar epidurography serves as an important radiographic procedure in the evaluation of patients with equivocal myelography and confusing or non-diagnostic physical findings. It is particularly valuable in patients with a wide ventral epidural space secondary to previous surgery, arachnoiditis or on a congenital basis. Several techniques and various contrast agents have been employed for the procedure. A pure Seldinger technique with a caudal approach through the sacral hiatus and injection of metrizamide gives excellent visualization of the epidural space and nerve root sleeves. The proper concentration of metrizamide is crucial for optimal results. Lateral, AP, and AP oblique radiographs, occasionally combined with lateral, complex motion tomography, clearly demonstrate the root sleeves and ventral epidural space. CT scanning, with present technology, does not provide the necessary detail for evaluating the epidural space.
TI Metrizamide lumbar epidurography with Seldinger technique through the sacral **notch** and selective nerve root injection.
SO Neuroradiology, (1980) 19/1 (19-25).
CODEN: NRDYAB
CT Medical Descriptors:
*epidurography

*intervertebral disk hernia
*lumbar spine
methodology
intrathecal drug administration
diagnosis
major clinical study
bone
cartilage
*meglumine iocarmate
*meglumine iotalamate
*metrizamide

L15 ANSWER 76 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 79113479 EMBASE
DOCUMENT NUMBER: 1979113479
TITLE: Inability to shut off a halothane vaporizer.
AUTHOR: Bjoraker D.G.
CORPORATE SOURCE: Dept. Anesthesiol., Univ. Michigan Med. Cent., Ann Arbor, Mich. 48109, United States
SOURCE: Anesthesiology, (1979) 50/1 (53-54).
CODEN: ANESAV
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
024 Anesthesiology
027 Biophysics, Bioengineering and Medical Instrumentation
LANGUAGE: English
AB Failure to cut off a halothane vaporizer occured because the plastic dial detent had worn down to the point where it escaped from its correct position. The detent normally provides the clicking sensation at each labeled position of the concentration selector dial by pushing a small plastic dowel against each **notch** in the lower rim of the dial as it is rotated. Since the worm detent was spring loaded, the assembly was then pushed against the underside of the concentration selector dial. There is a control arm fixed to the underside of the dial that normally engages the pin of a rotating drum outlet valve and closes the valve as 'off' when approached. In rotating the dial counterclockwise to shut off the vaporizer, this arm impinged on the detent assembly, preventing the dial from rotating below the 1.2 per cent halothane position.
SO Anesthesiology, (1979) 50/1 (53-54).
CODEN: ANESAV
AB . . . the clicking sensation at each labeled position of the concentration selector dial by pushing a small plastic dowel against each **notch** in the lower rim of the dial as it is rotated. Since the worm detent was spring loaded, the assembly. . .
CT Medical Descriptors:
*anesthesia
*anesthesia complication
*anesthetic equipment
*hazard
*vaporization
case report
inhalational drug administration
*halothane

L15 ANSWER 77 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 79011150 EMBASE
DOCUMENT NUMBER: 1979011150
TITLE: Implications of changes in amplitude and contour of the mercury strain gauge plethysmograph pulse tracing.
AUTHOR: Chandraratna P.A.N.; San Pedro S.; Schneider R.; et al.
CORPORATE SOURCE: Div. Cardiol., Univ. Oklahoma Hlth Sci. Cent., Oklahoma City, Okla., United States
SOURCE: British Heart Journal, (1978) 40/8 (907-910).
CODEN: BHJUAV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
027 Biophysics, Bioengineering and Medical Instrumentation
LANGUAGE: English
AB Alterations in the mercury strain gauge plethysmograph pulse tracing have been previously thought to denote changes in venous tone. This study was designed to define the implications of changes in amplitude and contour of pulse tracing. Seven normal subjects were studied. After control measurements, amyl nitrite was **administered** and the pulse tracing was recorded. When the haemodynamic state had returned to control levels 0.4 mg sublingual glyceryl trinitrate (GTN) was given. The amplitude of the plethysmograph pulse tracing (Y mm) and the vertical distance from the dicrotic **notch** to the peak of the pulse tracing (X mm) were measured. With amyl nitrite, the amplitude of the pulse tracing (Y) decreased from 10.4 .+-. 1 to 4.5 .+-. 0.6 mm (mean .+-. SEM), while the X/Y ratio increased from 0.7 .+-. 0.02 to 0.98 .+-. 0.02 (P<0.005). After GTN Y increased from 9.3 .+-. 0.8 to 31 .+-. 4.8 mm (P<0.005) and X/Y ratio increased from 0.7 .+-. 0.06 to 0.99 .+-. 0.01 (P<0.005). Since it is known that amyl nitrite produces venoconstriction and arteriolar dilatation, and GTN causes venous and arteriolar dilatation, we conclude that an increase in Y reflects venous dilatation, and an increase in X/Y ratio, that is a fall in the dicrotic **notch** , denotes arteriolar dilatation. Thus, the plethysmograph pulse tracing can be used to assess the effects of drugs on the capacitance and resistance beds.
SO British Heart Journal, (1978) 40/8 (907-910).
CODEN: BHJUAV
AB . . . of changes in amplitude and contour of pulse tracing. Seven normal subjects were studied. After control measurements, amyl nitrite was **administered** and the pulse tracing was recorded. When the haemodynamic state had returned to control levels 0.4 mg sublingual glyceryl trinitrate (GTN) was given. The amplitude of the plethysmograph pulse tracing (Y mm) and the vertical distance from the dicrotic **notch** to the peak of the pulse tracing (X mm) were measured. With amyl nitrite, the amplitude of the pulse tracing. . . an increase in Y reflects venous dilatation, and an increase in X/Y ratio, that is a fall in the dicrotic **notch**, denotes arteriolar dilatation. Thus, the plethysmograph pulse tracing can be used to assess the effects of drugs on the capacitance. . .

L15 ANSWER 78 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 78065631 EMBASE
DOCUMENT NUMBER: 1978065631
TITLE: [Rheumatoid polyarthritis in Black Africans (concerning 43 cases observed in Dakar)].

LA POLYARTHRITE RHUMATOIDE CHEZ LE NOIR AFRICAIN. (A PROPOS DE 43 CAS OBSERVES A DAKAR).
AUTHOR: Sankale M.; Sow A.M.; Diop B.; et al.
CORPORATE SOURCE: Clin. Med., Fac. Med. Pharm., Dakar, Senegal
SOURCE: Bulletin de la Societe Medicale d'Afrique Noire de Langue Francaise, (1976) 21/4 (443-454).
CODEN: BNLFA4
DOCUMENT TYPE: Journal
FILE SEGMENT: 031 Arthritis and Rheumatism
017 Public Health, Social Medicine and Epidemiology
005 General Pathology and Pathological Anatomy
LANGUAGE: French
AB Our series of 43 advanced cases of rheumatoid polyarthritis observed in Africans in Dakar included a definite feminine predominance (1 man to 3 women), having an average age of 35. The men were affected by the disease at a relatively older age than the women. As elsewhere, the attacking of the distal articulations of the upper limbs (wirsts and hands) is definitely more frequent than those of the articulations of the lower limbs (ankles and toes). Apart from subcutaneous nodules found in 9.3% of our cases, our series did not include any extra-articular attacks. Under the X-ray, the articular pinching is constant whereas decalcification was present 8 times out of 10 and **notches** 2 times out of 5. From the serological point of view, 31 cases were positive to Waaler-Rose reaction and/or to the latex test. 12 were negative. A comparison between the sero-positive and sero-negative forms tends to show a masculine predominance and a more favourable evolution in the latter group. On the whole this disease did not show any oddities in black Africans.
SO Bulletin de la Societe Medicale d'Afrique Noire de Langue Francaise, (1976) 21/4 (443-454).
CODEN: BNLFA4
AB . . . extra-articular attacks. Under the X-ray, the articular pinching is constant whereas decalcification was present 8 times out of 10 and **notches** 2 times out of 5. From the serological point of view, 31 cases were positive to Waaler-Rose reaction and/or to. . .
CT Medical Descriptors:
*race
*rheumatoid arthritis
*sex
ethnic or racial aspects
drug administration
major clinical study
sex difference

L15 ANSWER 79 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 78034821 EMBASE
DOCUMENT NUMBER: 1978034821
TITLE: The Cushing response as an anaesthesiological problem in neurosurgery.
AUTHOR: Fuchs E.C.
CORPORATE SOURCE: Neurosurg. Dept., Univ. Berlin, Germany
SOURCE: Journal of Neurosurgical Sciences, (1976) 20/3 (243-246).
CODEN: JNSSBV
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
024 Anesthesiology
003 Endocrinology
LANGUAGE: English
AB The exact neurological evaluation of different stages in acute midbrain herniation has made it possible to correlate severe clinical courses with therapeutic efforts. The Cushing response obviously appears in the late midbrain syndrome. A sudden increase of the ICP, which produces a pressure gradient between the supratentorial and the infratentorial space, is necessary to elicit this response. However anatomical differences in the size of the tentorial **notch** can produce an unpredictable discrepancy in the results. On admission 29 of 83 cases with a classical epidural hematoma showed the complete picture of a midbrain syndrome. After the immediate operative decompression 14 patients had signs of a bulbar syndrome. The analysis of the records enabled us to explain this deleterious outcome: In cases where Halothane was given, as the anesthetic agent, the originally elevated blood pressure (Cushing response) was already decreased before decompression, and the perfusion pressure became insufficient. Neuroleptanalgesia may also decrease the SAP as a result of the .alpha. receptor blockage.
SO Journal of Neurosurgical Sciences, (1976) 20/3 (243-246).
CODEN: JNSSBV
AB . . . supratentorial and the infratentorial space, is necessary to elicit this response. However anatomical differences in the size of the tentorial **notch** can produce an unpredictable discrepancy in the results. On admission 29 of 83 cases with a classical epidural hematoma showed. . .
CT Medical Descriptors:
*anesthesia
*blood pressure
*clinical study
*cushing reaction
*epidural hematoma
*mesencephalon syndrome
*neuroleptanalgesia
*neurosurgery
major clinical study
therapy
inhalational drug administration
diagnosis
*alfaxalone
*alfadolone acetate
*althesin
*diazepam
*fentanyl
*halothane
*ketamine
*neuroleptic agent
*nitrous oxide
*pancuronium bromide
*suxamethonium
*thiopental
*tubocurarine chloride

L15 ANSWER 80 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 76192784 EMBASE
DOCUMENT NUMBER: 1976192784
TITLE: [Assessment of functional peripheral vascular disturbance

with the 'nitroglycerine test'].
DER 'NITROGLYZERIN TEST' ZUR BEURTEILUNG FUNKTIONELLER PERIPHERER GEFASSSTORUNGEN.
AUTHOR: Boehme H.
CORPORATE SOURCE: Inst. Angiol., LVA Oberbayern, Munchen, Germany
SOURCE: Herz Kreislauf, (1975) 7/12 (666-671).
CODEN: HZKLAV
DOCUMENT TYPE: Journal
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
006 Internal Medicine
LANGUAGE: German
AB It is of clinical importance to differentiate between functional and organic vascular disturbance in acral circulation. This differentiation should distinguish vasospastic, i.e. functional, from truly occlusive, i.e. organic, symptoms. Further diagnostic and therapeutic measurements hinge on an accurate assessment of acral vascular disturbances. The 'nitroglycerine test' is of help in this differentiation. Acral volume pulse is registered every two minutes after oral application of 0.8 mg nitroglycerine. The change of the pulse curve, its shape and the form and timing of the dicrotic **notch** are all taken into consideration. This test is easily **administered**, repeated and evaluated.
SO Herz Kreislauf, (1975) 7/12 (666-671).
CODEN: HZKLAV
AB . . . of 0.8 mg nitroglycerine. The change of the pulse curve, its shape and the form and timing of the dicrotic **notch** are all taken into consideration. This test is easily **administered**, repeated and evaluated.

L15 ANSWER 81 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 76187578 EMBASE
DOCUMENT NUMBER: 1976187578
TITLE: Electrophysiological evidences for possible participation of periventricular neurons in anterior pituitary regulation.
AUTHOR: Kawakami M.; Sakuma Y.
CORPORATE SOURCE: Dept. Physiol., Yokohama City Univ. Sch. Med., Yokohama, Japan
SOURCE: Brain Research, (1976) 101/1 (79-94).
CODEN: BRREAP
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
002 Physiology
008 Neurology and Neurosurgery
030 Pharmacology
LANGUAGE: English
AB Unit activity of neurons in the periventricular area of the third ventricle (PVA), in which the organum vasculosum laminae terminalis is included, was recorded in female rats in proestrus. The units were antidromically driven by electrical stimulation of the arcuate median eminence region (ARC ME). In the antidromic responses, a **notch** was generally observed in the rising phase of the driven wave, and fractionation of A and B components at the **notch** was readily elicited by applying repetitive stimulatory pulses at frequencies higher than 10 Hz, or successive double pulses with intervals less than 3.5 msec. At the same time, ARC ME efferents to the PVA were suggested by orthodromic responses in the PVA to ARC ME stimulation. Occasionally, anti and orthodromic responses appeared in one electrode, indicating a proximate distribution of these two types of neurons in the PVA. Repetitive stimulation of the ARC ME at 50 Hz facilitated the orthodromically driven units, whereas antidromically driven units were inhibited. This seems to imply that the orthodromic responses might be recorded from an inhibitory interneuron in the ARC ME efferent pathway to the PVA, judging from the identical time course of the responses of the two types of the units. Both the anti and orthodromically driven units were tested with microiontophoresis of LH RH, TRH, LH, FSH and prolactin. Orthodromically driven units showed no response to microiontophoresis of any hormone. In the antidromically driven units, microiontophoresis of LH RH and FSH elicited inhibition in 15 and 18% of the tests, and facilitation was seen in 15-25% of the tests in response to LH, TRH and prolactin. The demonstration that local application of hypothalamic and pituitary hormones exerts direct effects on the activity of the PVA neurons which send their axons directly to the ARC ME, provides additional evidence that the PVA may participate in anterior pituitary regulation.
SO Brain Research, (1976) 101/1 (79-94).
CODEN: BRREAP
AB . . . units were antidromically driven by electrical stimulation of the arcuate median eminence region (ARC ME). In the antidromic responses, a **notch** was generally observed in the rising phase of the driven wave, and fractionation of A and B components at the **notch** was readily elicited by applying repetitive stimulatory pulses at frequencies higher than 10 Hz, or successive double pulses with intervals. . .
CT Medical Descriptors:
*adenohypophysis
*arcuate nucleus
*brain depth stimulation
*estrus
*hypothalamus
*iontophoresis
*median eminence
*rat
*brain third ventricle
theoretical study
topical drug administration
*follitropin
*luteinizing hormone
*gonadorelin
*prolactin
*thyrotropin
*protirelin

L15 ANSWER 82 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 76032489 EMBASE
DOCUMENT NUMBER: 1976032489
TITLE: Effect of adrenaline on the dynamic chloride current in cardiac Purkinje fibres.
AUTHOR: Hashimoto K.; Hauswirth O.; Ziskoven R.
CORPORATE SOURCE: Dept. Physiol. II, Univ. Bonn, Germany
SOURCE: PFLUG.ARCH.EUR.J.PHYSIOL., (1975) 355/Sup. (No. 35).
CODEN: PAGPA4
DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index
002 Physiology
LANGUAGE: English
AB The dynamic chloride current in cardiac Purkinje fibres was investigated by means of the voltage clamp technique. Earlier experiments showed that adrenaline (A) increases the amplitude of the dynamic chloride current (iCl), and increases the second slow inward current (iCa) in these preparations, and that the '**notch**' which is generated by the dynamic current reaches potentials considerably more negative than those reached with A **administration**. The inactivation kinetics of iCl are shifted in the depolarizing direction with A. The relation between the steady state degree of availability and the membrane potential (r (infinity)) is shifted by 7 mV and depressed in amplitude. The latter effect is most likely due to an increase of iCa caused by A. The time constant of removal of inactivation is accelerated by A from 570 msec to 430 msec. The beta blocker, ICI 66082, does not shift r (infinity) back t its original position but rather increases the amplitude of the curve again. An additional dose of 2x10-4 g/ml causes a further shift in the positive direction, to almost the same extent (6 mV), and again a depression of the amplitude. It is concluded that A effects iCl by influencing the electric field near the chloride channel whereas ICI 66082 as a beta blocker reduces iCa enhanced by the catecholamine.
SO PFLUG.ARCH.EUR.J.PHYSIOL., (**1975**) 355/Sup. (No. 35).
CODEN: PAGPA4
AB . . . of the dynamic chloride current (iCl), and increases the second slow inward current (iCa) in these preparations, and that the ' **notch**' which is generated by the dynamic current reaches potentials considerably more negative than those reached with A **administration**. The inactivation kinetics of iCl are shifted in the depolarizing direction with A. The relation between the steady state degree. . .

L15 ANSWER 83 OF 90 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 74162664 EMBASE
DOCUMENT NUMBER: 1974162664
TITLE: Osmotic opening of tight junctions in cerebral endothelium.
AUTHOR: Brightman M.W.; Hori M.; Rapoport S.I.; et al.
CORPORATE SOURCE: Lab. Neuropathol. Neuroanat. Scis, Nat. Inst. Neurol. Dis. Stroke, NIH, Bethesda, Md. 20014, United States
SOURCE: Journal of Comparative Neurology, (**1973**) 152/4 (317-325).
CODEN: JCNEAM
DOCUMENT TYPE: Journal
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
001 Anatomy, Anthropology, Embryology and Histology
LANGUAGE: English
AB Hyperosmotic solutions of 3 M urea, either infused into one internal carotid artery or applied topically to the pia mater of rabbits, cause the opening of endothelial tight junctions through which horseradish peroxidase passes from blood to extracellular fluid of the brain. The evidence for this opening of the blood brain barrier to protein is the entry of peroxidase into the extracellular pools between successive tight junctions. In animals not receiving 3 M urea, the interjunctional pools are inaccessible to proteins. Having passed through the endothelial junctions, the peroxidase spreads along the extracellular channels of the perivascular neuropil for approximately 100 .mu. in 90 sec. Most of the affected vessels are capillaries, though larger vessels are rendered leaky as well. Calyciform cisterns, that lie beneath shallow **notches** in the endothelium of untreated rabbits, appear to be enlarged after the **administration** of 3 M urea. It is undetermined whether these few endothelial cisterns and vesicles are involved in carrying protein from blood to the cerebral extracellular fluid.
SO Journal of Comparative Neurology, (**1973**) 152/4 (317-325).
CODEN: JCNEAM
AB . . . of the affected vessels are capillaries, though larger vessels are rendered leaky as well. Calyciform cisterns, that lie beneath shallow **notches** in the endothelium of untreated rabbits, appear to be enlarged after the **administration** of 3 M urea. It is undetermined whether these few endothelial cisterns and vesicles are involved in carrying protein from. . .

L15 ANSWER 84 OF 90 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:80300 BIOSIS
DOCUMENT NUMBER: PREV199395044800
TITLE: The linkage between stimulus frequency and covert peak areas as it relates to monaural localization.
AUTHOR(S): Rogers, Megan E.; Butler, Robert A. (1)
CORPORATE SOURCE: (1) Otolaryngol-Head Neck Surgery, Univ. Chicago Med. Cent., Box 412, 5841 S. Maryland Ave., Chicago, Ill. 60637 USA
SOURCE: Perception & Psychophysics, (1992) Vol. 52, No. 5, pp. 536-546.
ISSN: 0031-5117.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Head-related transfer functions for differently centered narrow noise bands were obtained on 6 subjects. Derived from these measurements were covert peak areas (CPAs), defined as the spatial constellation of loudspeakers that generates maximal sound pressure at the entrance of the ear canal for specific bands of frequency. On the basis of previous data, we proposed that different frequency bands served as important spectral cues for monaural localization of sounds from different loci and that location judgments were directed toward the CPAs associated with the different bands. In the first study, the stimuli were bandpass filtered so that they contained only those frequencies whose associated CPAs occupied either the monaural listener's "upper" or "lower" spatial regions. Loudspeakers, separated by 15 degree , were stationed in the left hemifield, ranging from 0 degree to 180 degree azimuth and -45 degree to 60 degree elevation. Subjects reported the loudspeaker from which the sound appeared to originate. Judgments of the sound's elevation were in general accord with the CPAs associated with the different frequency segments. In the second study, monaural localization tests were **administered** in which different 2.0-kHz-wide frequency bands linked with specific CPAs were **notch** filtered from a 3.5-kHz highpass noise band. For the control condition, the highpass noise was unfiltered. The data demonstrated that filtering a frequency segment linked with specific CPAs resulted in significantly fewer location responses directed toward that particular spatial region. These results demonstrate in greater detail the relation between the directional filtering properties of the pinna and monaural localization of sound.
SO Perception & Psychophysics, (1992) Vol. 52, No. 5, pp. 536-546.
ISSN: 0031-5117.

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L15 ANSWER 85 OF 90 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:307831 BIOSIS
DOCUMENT NUMBER: BA94:20981
TITLE: EFFECT OF ANABOLIC STEROIDS ON CRANIOFACIAL GROWTH AND DEVELOPMENT IN RATS.
AUTHOR(S): NODA K
CORPORATE SOURCE: GRADUATE SCH. DENT., OSAKA DENTAL UNIV., 5-31 OTEMAE 1-CHOME, CHUO-KU, OSAKA 540, JPN.
SOURCE: J OSAKA ODONTOL SOC, (1992) 55 (1), 72-81.
CODEN: SIGAAE. ISSN: 0030-6150.
FILE SEGMENT: BA; OLD
LANGUAGE: Japanese
AB Primary testosterone and its derivatives are anabolic steroids that are used in the treatment of osteoporosis and Turner syndrome. They also enhance first-twitch muscle weight in female rats. I evaluated the effect of an anabolic steroid on craniofacial growth and development in rats. One hundred and twenty 5-week-old female Sprague Dawley rats were divided into experimental and control groups. Rats in the experimental group were injected subcutaneously with 1 mg nandrolone phenylpropionate in the interscapular region on alternate days, while those in the control group were injected with a vehicle, arachis oil. The rats were sacrificed by chloroform at 60 and 120 days of age. Soft X-rays and cephalometric analysis showed that chronic **administration** of the anabolic steroid, nandrolone phenylpropionate, resulted in 1) about 20% increase in body weight, 2) an increase in total skull length, 3) elongation of the maxillary and mandibular incisors, 4) an increase in the depth of the anti-gonial **notch**, and 5) downward-forward growth of the viscerocranium against the neurocranium. These results suggest that nandrolone phenylpropionate accelerates craniofacial growth and development in rats.
SO J OSAKA ODONTOL SOC, (1992) 55 (1), 72-81.
CODEN: SIGAAE. ISSN: 0030-6150.
AB. . . rats were sacrificed by chloroform at 60 and 120 days of age. Soft X-rays and cephalometric analysis showed that chronic **administration** of the anabolic steroid, nandrolone phenylpropionate, resulted in 1) about 20% increase in body weight, 2) an increase in total skull length, 3) elongation of the maxillary and mandibular incisors, 4) an increase in the depth of the anti-gonial **notch**, and 5) downward-forward growth of the viscerocranium against the neurocranium. These results suggest that nandrolone phenylpropionate accelerates craniofacial growth and. . .

L15 ANSWER 86 OF 90 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1990:445205 BIOSIS
DOCUMENT NUMBER: BA90:95845
TITLE: A STUDY ON THE POSITION OF THE ANACROTIC AND DICROTIC **NOTCHES** ON THE ASCENDING AORTIC PRESSURE WAVE.
AUTHOR(S): IIDA N; TAKAZAWA K; UCHINO H; SETO T; MAEDA K; YABE K; HUJITA M; SAKAI T
CORPORATE SOURCE: DEP. INTERN. MED. TOKYO MED. COLL.
SOURCE: J TOKYO MED COLL, (1990) 48 (3), 350-360.
CODEN: TIDZAH. ISSN: 0040-8905.
FILE SEGMENT: BA; OLD
LANGUAGE: Japanese
AB The aim of this study was to evaluate the relationships between the positions of the anacrotic and dicrotic **notches** on the ascending aortic pressure wave, and changes in blood pressure. Eighty-five patients (55 .+-. 8: mean .+-. 1 SD), 36 with myocardial infarction (MI group), 37 with angina pectoris (AP group) and 12 others (OT group) were studied. There were no statistical differences between the mean age of the groups. Ascending aortic pressure and its first derivative, which clearly showed the position of the anacrotic **notch**, were found using a micromanometer-tipped catheter (Millar-PC-484A) in the normal condition, and after an intravenous injection of 2.5 micrograms angiotensin and a sublingual **administration** of 0.3 mg nitroglycerin. There were no statistical differences between the mean systolic and diastolic pressures of the groups. The two ratios derived were the anacrotic **notch** ratio (ANR) and dicrotic **notch** ratio (DNR): ANR = (late peak aortic systolic pressure - pressure at anacrotic **notch**)/(pulse pressure) .times. 100(%); DNR = (late peak aortic systolic pressure - pressure at dicrotic **notch**)/(pulse pressure) .times. 100(%). ANR was 38.1 .+-. 10.7% in the MI group, 35.9 .+-. 13.3% in the AP group and 31.8 .+-. 10.8% in the OT group. ANR was higher in the MI group than in the OT group, which suggests that arterial wall sclerosis was greater in the myocardial infarction patients even though the mean ages of the groups were not significantly different. DNR was 37.9 .+-. 11.6% in the MI group, 36.6 .+-. 7.4% in the AP group and 35.6 .+-. 9.9 in the OT group. These values were not significantly different. ANR increased with blood pressure. DNR increased with heart rate but not with blood pressure. Angiotensin produced a significant increase in ANR but no change in DNR. Nitroglycerin produced a significant decrease in ANR and an increase in DNR. ANR is influenced by organic changes in the arterial wall and functional changes in blood pressure, whereas DNR is influenced by heart rate.
TI A STUDY ON THE POSITION OF THE ANACROTIC AND DICROTIC **NOTCHES** ON THE ASCENDING AORTIC PRESSURE WAVE.
SO J TOKYO MED COLL, (1990) 48 (3), 350-360.
CODEN: TIDZAH. ISSN: 0040-8905.
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L15 ANSWER 87 OF 90 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1990:6677 BIOSIS
DOCUMENT NUMBER: BA89:6677
TITLE: SYNAPTOLOGY OF THE CLAUSTRUM IN THE RAT.
AUTHOR(S): TREVISI M; RICCI D; BIGONI R
CORPORATE SOURCE: IST. DI ANAT. UMANA NORMALE, VIA FOSSATO DI MORTARA, 66, 44100 FERRARA.
SOURCE: ARCH ITAL ANAT EMBRIOL, (1989) 94 (1), 85-90.
CODEN: AIAEA2. ISSN: 0004-0223.
FILE SEGMENT: BA; OLD
LANGUAGE: Italian

AB A great deal of information is available on the morphology of the claustrum in various animal species, as well as on its neuronal distribution and relationships with cerebral cortex and other nuclei. However, no research has been performed on synaptic organization. Here we report an ultrastructural study performed on 7 male albino rats of the Wistar strain weighing 270-310 g. Five rats were sacrificed by prolonging general anesthesia with diethyl ether until death. Three of these rats were secured to the stereotaxic atlas corrdinates of Paxinos and Watson (1982), the claustrum area was marked injecting 1 .mu.l of a 10% Evans Blue solution into the nucleus. The brain was then removed from the skull, cut in 2-3 mm thick coronal sections, and tissue samples taken from the area immediately adjacent to the marked area, were immersed in 2% OsO4 buffered with 2% potassium dichromate containing 0.2% CaCl2 at pH 7.7 (Gobel, 1968). After dehydration they were embedded in Durcupan and the ultrafine sections were stained with uranyl acetate and lead citrate and observed with either a Zeiss 9S2 or a Hitachi H 800 electron microscope. The samples from two other rats, taken with the stereotaxic techniques described, were fixed for 12 h in 0.6 potassium permanganate solution buffered with veronal-acetate at pH 7.4 (Luft, 1956). After processing for the electron microscopy, a portion of the sections were used without any contrast medium and the remainder were stained with uranyl acetate and lead citrate. Two more rats were anesthetized with the endoperitoneal **administration** of Ketalar (Parke-Davis) at a dose of 70 mg/Kg b.w. and fixation was performed by transcardiac perfusion with 3% glutaraldehyde in a 0.1 M phoshpate buffer pH 7.4. The brain was cut and immersed 3 h in 3% glutaraldehyde in the same buffer. By using a stereomicroscope and the above mentioned stereotaxic atlas, the area of the claustrum was identified in the region where the nucleus achieves its greatest dimensions and is limited both above and medially by the marked **notch** of the corpus callosium. After washing in 0.3 M sucrose in the same buffer, the blocks were fixed again in 1.5% buffered OsO4, transferred to a 2% aqueous solution of uranyl acetate, dehydrated in ethanol and embedded in Durcupan (Etcheverry and Pellegrino De Iraldi, 1968). Morphometric analysis was performed with a Zeiss IBAS I semi-authomatic image analyzer on both high (84.000X) and low (5.400X) magnification micrograhs. The parameters collected at high magnification were: the length of active synaptic zones, the form factor to define circular or elliptic or irregular structures, the maximum diameter of the synaptic vesicles and the widths of the synaptic cleft. To evaluate the relationship between the different types of synapses, the large field and low magnifiction micrographs were examined with a stereomicroscope. According to the morphology of the synaptic terminals and the type of synaptic vesicles, the synaptology of the nucleus appears quite uniform. In each sample asymmetrical synapses (Type I) are largely prevalent (10:1 ratio) involving the neuronal soma, dendritic trunks and dendritic spines. The most interesting feature emerging from the study performed is the presence of a mixed population of synaptic vesicles within the same terminal bag (mixed in terms of shape, size and electron density). These evidences are consistent with the hypothesis that multiple neurotransmitters, coexists, even though their specific nature remains to be determined. Absent from the samples examined were vesicles with a central dense-core clearly separated from the limiting membrane.
SO ARCH ITAL ANAT EMBRIOL, (1989) 94 (1), 85-90.
CODEN: AIAEA2. ISSN: 0004-0223.
AB. . . medium and the remainder were stained with uranyl acetate and lead citrate. Two more rats were anesthetized with the endoperitoneal **administration** of Ketalar (Parke-Davis) at a dose of 70 mg/Kg b.w. and fixation was performed by transcardiac perfusion with 3% glutaraldehyde. . . in the region where the nucleus achieves its greatest dimensions and is limited both above and medially by the marked **notch** of the corpus callosium. After washing in 0.3 M sucrose in the same buffer, the blocks were fixed again in. . .

L15 ANSWER 88 OF 90 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1989:382557 BIOSIS
DOCUMENT NUMBER: BA88:63147
TITLE: PARAPHARYNGEAL ABSCESS DUE TO AN IMPACTED THIRD MOLAR AT THE MANDIBULAR **NOTCH**.
AUTHOR(S): SHIONO H
CORPORATE SOURCE: DEP. OTOLARYNGOL., TOKYO UNIV. BRANCH HOSP., TOKYO.
SOURCE: JIBI INKOKA TOKEIBU GEKA, (1989) 61 (5), 389-393.
CODEN: JITGE2.
FILE SEGMENT: BA; OLD
LANGUAGE: Japanese

AB Infections of the parapharyngeal space, also known as deep neck abscesses, draw a special attention because of life threatening complications than may follow if treatment is delayed or inadequate. A 35-year-old male had experienced a swelling and spontaneous pain of the right submandibular area. X-ray examination showed an impacted third molar, and CT scan showed an impacted third molar, and CT scan showed a low density lesion of the parapharyngeal space accompanied with deformity. The right parapharyngeal abscess caused by an impacted third molar at the mandibular **notch** was diagnosed. Intra-oral incision was made and the parapharyngeal space was drained under systemic **administration** of antibiotics. Discussion was made for anatomical, bacteriological, and diagnostic aspects of parapharyngeal abscess.
TI PARAPHARYNGEAL ABSCESS DUE TO AN IMPACTED THIRD MOLAR AT THE MANDIBULAR **NOTCH**.
SO JIBI INKOKA TOKEIBU GEKA, (1989) 61 (5), 389-393.
CODEN: JITGE2.
AB. . . of the parapharyngeal space accompanied with deformity. The right parapharyngeal abscess caused by an impacted third molar at the mandibular **notch** was diagnosed. Intra-oral incision was made and the parapharyngeal space was drained under systemic **administration** of antibiotics. Discussion was made for anatomical, bacteriological, and diagnostic aspects of parapharyngeal abscess.

L15 ANSWER 89 OF 90 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1988:290401 BIOSIS
DOCUMENT NUMBER: BA86:18668
TITLE: THREE RECENT CASES OF ASCARIASIS IN NORTHERN KYUSHU JAPAN.
AUTHOR(S): MAKIYA K; TSUKAMOTO M; UNOKI H; SUJITA K; MORI N; MIKI T;

YOKOYAMA M
CORPORATE SOURCE: DEP. MED. ZOOL., SCH. MED., UNIV. OCCUPATIONAL ENVIRON. HEALTH, KITAKYUSHU 807, JPN.
SOURCE: J UOEH, (1988) 10 (1), 123-132.
CODEN: JOUOD4. ISSN: 0387-821X.
FILE SEGMENT: BA; OLD
LANGUAGE: Japanese
AB Ascariasis is considered to be one of the rare infectious diseases in Japan, but recently it has been slightly increasing. This paper reports three ascariasis cases who seemed to be infected recently in the Kitakyushu area, Japan. Case 1: A 59-year-old woman in Kitakyushu City passed a round worm after continuous abdominal pain. The patient was discharged from the hospital because of no further abnormal intestinal symptoms and findings. Case 2: An 85-year-old woman in Nakama City, who suffered from cerebral infarction, vomited a round worm before hospitalization. Many ascarid eggs were detected after admission, and after treatment with pyrantel pamoate (Combantrin) two round worms were passed and egg detection became negative. Case 3: A 77-year-old man in Saikawa Town vomited 3 round worms after gastrectomy due to early gastric cancer. Many unfertilized eggs were also detected from the stool together with hook worm eggs, but no eggs were found after **administration** of pyrantel pamoate. Morphological examination was made by a scanning electron microscope on the denticles on the dentigerous lip ridges of the worms to differentiate from possible infection with a pig parasite, Ascaris suum. The three cases were diagnosed as ascariasis due to human Ascaris lumbricoids based on the following evidences that the expelled worms had 1) less pointed tips of the denticles and shallower or wider interdenticle **notches**, and 2) far more denticles of smaller size along the dentigerous ridges, compared with Ascaris suum. The necessity of differentiating pig- from human-ascarids, when considering human infection with Ascaris suum is discussed.
SO J UOEH, (1988) 10 (1), 123-132.
CODEN: JOUOD4. ISSN: 0387-821X.
AB. . . Many unfertilized eggs were also detected from the stool together with hook worm eggs, but no eggs were found after **administration** of pyrantel pamoate. Morphological examination was made by a scanning electron microscope on the denticles on the dentigerous lip ridges. . . the following evidences that the expelled worms had 1) less pointed tips of the denticles and shallower or wider interdenticle **notches**, and 2) far more denticles of smaller size along the dentigerous ridges, compared with Ascaris suum. The necessity of differentiating. . .

L15 ANSWER 90 OF 90 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1985:258365 BIOSIS
DOCUMENT NUMBER: BA79:38361
TITLE: EXPERIMENTS ON INTERSPECIFIC HYBRIDIZATION BETWEEN ORYZIAS-LATIPES AND ORYZIAS-CELEBENSIS.
AUTHOR(S): IWAMATSU T; UWA H; INDEN A; HIRATA K
CORPORATE SOURCE: DEP. BIOL., AICHI UNIV. EDUC., KARIYA 448, JAPAN.
SOURCE: ZOOL SCI (TOKYO), (1984) 1 (4), 653-664.
CODEN: ZOSCEX.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Artificial interspecific fertilization of O. latipes eggs by O. celebensis sperm and the reciprocal cross were successful. The hybrids, O. latipes celebensis, which had a single set of each parental genome, were reared until they reached the adult stage with a survival rate similar to that of the controls. In 63 hybrids, some morphological characteristics were grossly intermediate between the parental types while others were O. celebensis in type. Only the rate of increase in ray node numbers and **notches** in the anal and dorsal fins of the male were like O. latipes. Two of the 33 hybrid females were induced to spawn every day by O. celebensis males. Ten of the hybrid males examined were sterile (testes lacked spermatozoa) and the remaining 20 were neuters (gonads not recognizable). Some sexual characteristics became conspicuous in the hybrids upon **administration** of sex hormones, but formation of horny processes in the anal fin ray was not induced. All digenomous triploid hybrids resulting from backcrossing of O. latipes celebensis (eggs) to O. celebensis (spermatozoa) died at the embryonic stage of initial blood circulation.
SO ZOOL SCI (TOKYO), (1984) 1 (4), 653-664.
CODEN: ZOSCEX.
AB. . . the parental types while others were O. celebensis in type. Only the rate of increase in ray node numbers and **notches** in the anal and dorsal fins of the male were like O. latipes. Two of the 33 hybrid females were. . . lacked spermatozoa) and the remaining 20 were neuters (gonads not recognizable). Some sexual characteristics became conspicuous in the hybrids upon **administration** of sex hormones, but formation of horny processes in the anal fin ray was not induced. All digenomous triploid hybrids. . .

```
=> Lamb R?/au or Dallman M?/au or Hoyne G?/au
LAMB IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s Lamb R?/au or Dallman M?/au or Hoyne G?/au
L16       3448 LAMB R?/AU OR DALLMAN M?/AU OR HOYNE G?/AU

=> sl16 and (notch)
SL16 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l16 and (notch)
L17         26 L16 AND (NOTCH)

=> dup rem l17
PROCESSING COMPLETED FOR L17
L18          11 DUP REM L17 (15 DUPLICATES REMOVED)

=> dis l18 1-11 ibib abs

L18 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER:       2002:123354 CAPLUS
TITLE:                  Assay
INVENTOR(S):            Lamb, Jonathan Robert; Hoyne, Gerard Francis
                        ; Dallman, Margaret Jane; Champion, Brian
                        Robert
PATENT ASSIGNEE(S):     Lorantis Limited, UK
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SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012890	A2	20020214	WO 2001-GB3503	20010803

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-19242 A 20000804
AB A method for monitoring the immune system comprising monitoring the **Notch** signalling pathway.

L18 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:380426 CAPLUS
DOCUMENT NUMBER: 135:9978
TITLE: Immunotherapy with genetically engineered tumor-infiltrating lymphocytes
INVENTOR(S): Lamb, Jonathan Robert; **Hoyne, Gerard Francis**
PATENT ASSIGNEE(S): Lorantis Ltd., UK
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001035990	A2	20010525	WO 2000-GB4391	20001117

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-27328 A 19991118
AB A method is provided for enhancing the reactivity of a T cell toward a tumor cell which method comprises: (a) isolating a T cell which is a tumor-infiltrating lymphocyte (TIL) from a patient having said tumor cell present in their body; (b) introducing a nucleic acid sequence into the TIL, which sequence is capable of inhibiting or preventing expression of an endogenous **Notch** ligand in the TIL; and (c) re-introducing the transfected TIL into the patient; wherein the T cell comprises a T cell receptor specific for a tumor antigen expressed by the tumor cell.

L18 ANSWER 3 OF 11 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001677038 MEDLINE
DOCUMENT NUMBER: 21579863 PubMed ID: 11722637
TITLE: **Notch** signalling in the regulation of peripheral immunity.
AUTHOR: **Hoyne G F**; **Dallman M J**; Champion B R; Lamb J R
CORPORATE SOURCE: Immunobiology Group, Department of Pathology, Respiratory Medicine Unit, MRC Centre of Inflammation Research, University of Edinburgh, Edinburgh, UK.. g.hoyne@ed.ac.uk
SOURCE: IMMUNOLOGICAL REVIEWS, (2001 Aug) 182 215-27. Ref: 81
Journal code: 7702118. ISSN: 0105-2896.
PUB. COUNTRY: Denmark
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20011128
Last Updated on STN: 20020209
Entered Medline: 20020208
AB **Notch** signalling plays a critical role in embryogenesis, influencing the differentiation and growth of a variety of cell types across the species. In the mammalian immune system, **Notch** signalling operates at various levels; it controls the differentiation of haematopoietic stem cells and directs the early development of the T and B-cell lineages. It is also involved in the maturation of both CD4+ and CD8+ T cells in the thymus. The biological activities of this pathway extend beyond lymphocyte ontogeny; recent evidence has shown that it also contributes to the regulation of the peripheral immune system through its ability to influence cell survival and growth. In fulfilling this function, **Notch** signalling appears to act in conjunction with defined immunological signals such as cytokines, T-cell antigen receptor and co-stimulatory receptor-mediated signalling. In this review we discuss the potential of the **Notch** signalling pathway in the maintenance of homeostasis within the immune system affecting both peripheral tolerance and the negative feedback controlling productive immunity. The therapeutic manipulation of this pathway is likely to have broad application in a range of immunologically based diseases.

L18 ANSWER 4 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:178247 BIOSIS
DOCUMENT NUMBER: PREV200100178247
TITLE: Regulatory T cells: A role for **notch** signalling.
AUTHOR(S): Lamb, J. (1); **Dallman, M. J. (1)**; **Hoyne, G. F. (1)**
CORPORATE SOURCE: (1) University of Edinburgh and Imperial College of Science, Technology and Medicine, London UK
SOURCE: Clinical and Experimental Allergy, (January, 2001) Vol. 31, No. 1, pp. 165. print.
Meeting Info.: Annual Meeting of the British Society for Allergy and Clinical Immunology Nottingham, England August 02-03, 2000 British Society for Allergy and Clinical

Immunology
. ISSN: 0954-7894.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L18 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:421290 CAPLUS
DOCUMENT NUMBER: 133:72935
TITLE: Methods of immunosuppression
INVENTOR(S): Lamb, Jonathan Robert; **Dallman, Margaret Jane** ; **Hoyne, Gerard Francis**
PATENT ASSIGNEE(S): Lorantis Ltd., UK
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000036089	A2	20000622	WO 1999-GB4233	19991215
WO 2000036089	A3	20001026		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1141243	A2	20011010	EP 1999-961206	19991215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001048930	A1	20011206	US 2001-870902	20010531

PRIORITY APPLN. INFO.: GB 1998-27604 A 19981215
WO 1999-GB4233 W 19991215

AB A method for producing a T cell having tolerance to an allergen or antigen which method comprises incubating the T cell with an antigen presenting cell (APC) in the presence of (i) a compn. capable of upregulating expression of an endogenous **Notch** ligand in the APC and (ii) the allergen or antigen is provided. The **Notch** or **Notch** ligand-upregulating compn. comprises a polypeptide selected from Noggin, Chordin, Follistatin, Xnr3, FGF or deriv.; and an immunosuppressive cytokine selected from IL-4, IL-10, IL-13, TGF-.beta. and FLT3.

L18 ANSWER 6 OF 11 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000404250 MEDLINE
DOCUMENT NUMBER: 20387636 PubMed ID: 10929049
TITLE: T-cell regulation of peripheral tolerance and immunity: the potential role for **Notch** signalling.
AUTHOR: **Hoyne G F**; **Dallman M J**; Lamb J R
CORPORATE SOURCE: Immunobiology Group, MRC Centre for Inflammation Research and the Respiratory Medicine Unit, University of Edinburgh, Teviot Place, Edinburgh, UK.
SOURCE: IMMUNOLOGY, (2000 Jul) 100 (3) 281-8. Ref: 36
Journal code: GH7; 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000901
Last Updated on STN: 20000901
Entered Medline: 20000821

AB Recognition of antigen by T cells in the periphery may lead either to the generation of productive immunity or the induction of tolerance. These two functional outcomes are a consequence of distinct pathways of T-cell differentiation. T cells are selected to become regulatory cells and their function is to maintain homeostasis with the immune system. In this review we discuss the cell-fate decisions that T cells might make allowing them to promote immunity or induce tolerance in the context of the role that **Notch** signalling may play in this process.

L18 ANSWER 7 OF 11 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2000120669 MEDLINE
DOCUMENT NUMBER: 20120669 PubMed ID: 10653853
TITLE: Serrate1-induced **notch** signalling regulates the decision between immunity and tolerance made by peripheral CD4(+) T cells.
AUTHOR: **Hoyne G F**; Le Roux I; Corsin-Jimenez M; Tan K; Dunne J; Forsyth L M; **Dallman M J**; Owen M J; Ish-Horowicz D; Lamb J R
CORPORATE SOURCE: Respiratory Medicine Unit, University of Edinburgh Medical School, Teviot Place, Edinburgh EH8 9AG, UK.
SOURCE: INTERNATIONAL IMMUNOLOGY, (2000 Feb) 12 (2) 177-85.
Journal code: AY5; 8916182. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000505
Last Updated on STN: 20000505
Entered Medline: 20000424

AB Signals derived from antigen-presenting cells (APC) influence the functional differentiation of CD4(+) T cells. We report here that Serrate1 (Jagged1), a ligand for the Notch1 receptor, may contribute to the differentiation of peripheral CD4(+) T cells into either helper or regulatory cells. Our findings demonstrate that antigen presented by murine APC overexpressing human Serrate1 induces naive peripheral CD4(+) T cells to become regulatory cells. These cells can inhibit primary and secondary immune responses, and transfer antigen-specific tolerance to recipient mice. Our results show that **Notch** signalling may help explain 'linked' suppression in peripheral tolerance, whereby tolerance induced to one epitope encompasses all epitopes on that antigen during the course of an immune response.

L18 ANSWER 8 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:82870 BIOSIS
DOCUMENT NUMBER: PREV200100082870
TITLE: Use of conditional transgenic mice to study the role of **Notch** signaling in T cells.
AUTHOR(S): Tan, Karen (1); Lamb, Jonathan R. (1); **Hoyne, Gerard F. (1)**
CORPORATE SOURCE: (1) Immunobiology Group, MRC Centre for Inflammation Research, University of Edinburgh Medical School, Teviot Place, Edinburgh, EH8 9AG UK
SOURCE: Immunology, (December, 2000) Vol. 101, No. Supplement 1, pp. 20. print.
Meeting Info.: Annual Congress of the British Society for Immunology Harrogate, UK December 05-08, 2000 British Society for Immunology
. ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L18 ANSWER 9 OF 11 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1999242412 MEDLINE
DOCUMENT NUMBER: 99242412 PubMed ID: 10224357
TITLE: Linked suppression in peripheral T cell tolerance to the house dust mite derived allergen Der p 1.
AUTHOR: **Hoyne G F**; **Dallman M J**; Lamb J R
CORPORATE SOURCE: Respiratory Medicine Unit, Edinburgh University Medical School, Edinburgh, UK.
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1999 Feb-Apr) 118 (2-4) 122-4.
Journal code: BJ7; 9211652. ISSN: 1018-2438.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990618
Last Updated on STN: 19990618
Entered Medline: 19990610

AB BACKGROUND: Peripheral tolerance is required to maintain balance within the immune system. A feature of peripheral tolerance is linked suppression, in which tolerance induced to a single T cell epitope inhibits the response to all epitopes in the same protein. It is suggested that this phenomenon is mediated by regulatory T cells through either the activity of immunopressive cytokines or direct cell contact. In previous experiments we failed to detect inhibitory cytokines when T cells from mice rendered tolerant by intranasal delivery of the immunodominant peptide of Der p 1 (p 1, 110-131) were restimulated with peptide in vitro. Therefore, the aim of this study was to determine if cognate interactions between T cells mediated by **Notch**/Delta signaling induce and maintain peripheral T cell tolerance. METHODS: Using in situ hybridization and viral mediated gene transfer, the expression and function of Delta1 were investigated in a murine model of T cell tolerance to Der p 1 in vivo. RESULTS: Delta1 expression is increased on peripheral T cells during the induction of tolerance with high-dose peptide delivered intranasally and when tolerant animals are rechallenged under immunogenic conditions. Peptide p 1, 110-131-specific CD4+ T cells transfected with Delta1 inhibited the response of antigen-primed T cells and induced linked suppression. CONCLUSIONS: High-dose peptide delivered intranasally induces transient expression of Delta 1 on inhibitory CD4+ T cells. Ligation of the Notch1 receptor on neighbouring T cells by Delta1+ regulatory T cells inhibits clonal expansion of the former and mediates linked suppression.

L18 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:324898 CAPLUS
DOCUMENT NUMBER: 128:320575
TITLE: Controlling abnormal immune responses by modulation of the interactions between members of the **Notch** family of proteins
INVENTOR(S): Lamb, Jonathan Robert; **Dallman, Margaret Jane**; **Hoyne, Gerald Francis**
PATENT ASSIGNEE(S): Imperial College of Science Technology & Medicine, UK; Lamb, Jonathan Robert; Dallman, Margaret Jane; Hoyne, Gerald Francis
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9820142	A1	19980514	WO 1997-GB3058	19971106
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9748765	A1	19980529	AU 1997-48765	19971106
AU 736361	B2	20010726		
GB 2335194	A1	19990915	GB 1999-10276	19971106
GB 2335194	B2	20010425		
EP 942998	A1	19990922	EP 1997-911353	19971106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1242802	A	20000126	CN 1997-181159	19971106
GB 2353094	A1	20010214	GB 2000-23691	19971106
GB 2353094	B2	20010613		
JP 2001504331	T2	20010403	JP 1998-521150	19971106
NO 9902196	A	19990705	NO 1999-2196	19990505

PRIORITY APPLN. INFO.:	GB 1996-23236	A	19961107
	GB 1997-15674	A	19970724
	GB 1997-19350	A	19970911
	GB 1999-10276	A3	19971106
	WO 1997-GB3058	W	19971106

AB Methods of modifying the interaction of components such as T-cells, T-cell-antigen presenting cells (APC) and between pathogenic organisms and immunocompetent cells of a host using members of the **Notch** protein family and their ligands are described. Hybridoma cells expressing the gene for Delta protein were shown to prevent antigen-primed

lymphocytes from proliferating upon exposure to the priming antigen. Dendritic cells expressing the Serrate gene prevented the antigen priming of T cells. The use T cell hybridomas expressing the Delta gene to inhibit the development of immunity to the Der p 1 is demonstrated.

L18 ANSWER 11 OF 11 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1998384211 MEDLINE
DOCUMENT NUMBER: 98384211 PubMed ID: 9716576
TITLE: Stromal expression of Jagged 1 promotes colony formation by fetal hematopoietic progenitor cells.
AUTHOR: Jones P; May G; Healy L; Brown J; **Hoyne G**; Delassus S; Enver T
CORPORATE SOURCE: Section of Gene Function and Regulation & Leukaemia Research Fund Centre, Chester Beatty Laboratories, Institute of Cancer Research, London, UK.
SOURCE: BLOOD, (1998 Sep 1) 92 (5) 1505-11.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 20000303
Entered Medline: 19980910

AB The **Notch** signaling system regulates proliferation and differentiation in many tissues. **Notch** is a transmembrane receptor activated by ligands expressed on adjacent cells. Hematopoietic stem cells and early progenitors express **Notch**, making the stromal cells which form cell-cell contacts with progenitor cells candidate ligand-presenting cells in the hematopoietic microenvironment. Therefore, we examined primary stromal cell cultures for expression of **Notch** ligands. Using reverse transcription-polymerase chain reaction, in situ hybridization, immunohistochemistry, and Western blotting, we demonstrate expression of Jagged 1 in primary stromal cultures. To investigate if the stromal expression of Jagged 1 has functional effects on hematopoietic progenitors, we cultured CD34(+), c-kit+ hematopoietic progenitor cells derived from the aorto gonadal mesonephros region of day 11 mouse embryos on the Jagged 1(-) stromal cell line S17 and on S17 cells engineered to express Jagged 1. The presence of Jagged 1 increased the number of colonies formed in subsequent methylcellulose culture fourfold. Larger increases in colony numbers were observed under the same culture conditions with CD34(+), c-kit+ hematopoietic progenitor cells derived from d11 fetal liver. These results obtained in vitro table Jagged 1 as a candidate regulator of stem cell fate in the context of stromal microenvironments in vivo.

=> s adamalysin
L19 156 ADAMALYSIN

=> Dis l19 -10 kwic

L19 ANSWER 1 OF 156 MEDLINE
AB . . . role in joint articular tissue degeneration. Additional enzymes of the metalloprotease family, such as the membrane-type metalloproteases (MT-MMPs) and the **adamalysins** that include the ADAMs and the ADAMTS families, have also been found to be involved in these disease processes. At. . .

L19 ANSWER 2 OF 156 MEDLINE
AB . . . An example, based on five mammalian and fungal matrix metalloproteinase crystal structures (human fibroblast collagenase, neutrophil collagenase, stromelysin, astacin, and **adamalysin**), illustrates a number of features of the Gaussian-based approach.

L19 ANSWER 3 OF 156 MEDLINE
TI Three-dimensional structure of fibrolase, the fibrinolytic enzyme from southern copperhead venom, modeled from the X-ray structure of **adamalysin** II and atrolysin C.
AB . . . of conserved and variable sequences between members of the snake venom metalloproteinases. When compared to atrolysin C (form D) or **adamalysin** II (metzincins with completely different substrate specificity), fibrolase has approximately 60% overall sequence identity and nearly 100% sequence similarity in the active site. We used the crystal structure of **adamalysin** II to build a 3-dimensional homology model of fibrolase. Three disulfide bonds were constructed (the highly conserved disulfide bond [118-198] was maintained from the **adamalysin** II structure and 2 new disulfide bonds were introduced between residues 158-182 and 160-165). We used Sculpt 2.5 and HyperChem. . .
CN 0 (Oligopeptides); 0 (Viper Venoms); EC 3.4.24 (Metalloendopeptidases); EC 3.4.24.- (fibrolase); EC 3.4.24.42 (atrolysin C); EC 3.4.24.46 (**adamalysin**)

L19 ANSWER 4 OF 156 MEDLINE
AB . . . of pro-TNF-alpha, along with a homology model of the catalytic domain of TACE based on the X-ray diffraction coordinates of **adamalysin**, we synthesized N-hydroxyformamide TACE inhibitors containing a P2' arginine side chain. Introduction of nitro and sulfonyl electron-withdrawing groups covalently bound. . .

L19 ANSWER 5 OF 156 MEDLINE
TI Inhibitory antibodies against endopeptidase activity of human **adamalysin** 19.
AB Human **adamalysin** 19 (hADAM19)/meltrin beta is a member of the ADAM (a disintegrin and metalloproteinase) family and an active metalloproteinase. It is a new metalloproteinase and disintegrin dendritic cell antigen marker. **Adamalysin** 19 gene was expressed in normal and transformed tissues and cells such as placenta, brain, heart, leukocytes, and colorectal adenocarcinoma. . .

L19 ANSWER 6 OF 156 MEDLINE
AB . . . carboxylates, highly constrained analogues of endogenous pyroglutamyl tripeptide inhibitors of snake venom endopeptidases, have been prepared as potential inhibitors of **adamalysin** II and matrix metalloproteinases. They proved to be inactive against **adamalysin** II and weak inhibitors of gelatinase A, gelatinase B, stromelysin 1 and human neutrophil collagenase. Evaluation of the mode of binding of the (2R,5S,11bR) isomer in the active site of **adamalysin** II suggests that the decrease of potency may be due to the reorientation of the acylamino chain in three of. . .

L19 ANSWER 7 OF 156 MEDLINE
AB ADAMTS proteinases, belonging to the **adamalysin** subfamily of metalloproteinases, have been implicated in a variety of cellular events such as morphogenesis, cell migration, angiogenesis, ovulation and. . .

L19 ANSWER 8 OF 156 MEDLINE
AB The **adamalysins** are involved in proteolysis, adhesion, fusion, and intracellular signaling. Human ADAM19/**adamalysin**-19 (A disintegrin and metalloproteinase 19) was identified from primary dendritic cell cDNA libraries. It has a signal sequence, a pro-domain. .

L19 ANSWER 9 OF 156 MEDLINE
AB . . . characteristics sequences H142E143XXH146XXG149XXH152 and C164I165M166. The three-dimensional structure of neuwiedase was modeled based on the crystal structure of Crotalus adamanteus **Adamalysin** II. This model revealed that the zinc binding site region showed a high structural similarity with other metalloproteases. The proteolyitc. . .

L19 ANSWER 10 OF 156 MEDLINE
AB . . . 15 min after insemination. Tissue inhibitor of metalloprotease-3 and Ro 31-9790, specific inhibitors of zinc metalloproteases in the matrixin and **adamalysin** families, also inhibited sperm-egg fusion but not sperm-egg binding. These data indicate a role in gamete fusion for one or more zinc metalloproteases of the matrixin and/or **adamalysin** families that act after plasma membrane binding and before sperm-egg membrane fusion.

=> end
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NEWS 2	Sep 17	IMSworld Pharmaceutical Company Directory name change to PHARMASEARCH
NEWS 3	Oct 09	Korean abstracts now included in Derwent World Patents Index
NEWS 4	Oct 09	Number of Derwent World Patents Index updates increased
NEWS 5	Oct 15	Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS 6	Oct 22	Over 1 million reactions added to CASREACT
NEWS 7	Oct 22	DGENE GETSIM has been improved
NEWS 8	Oct 29	AAASD no longer available
NEWS 9	Nov 19	New Search Capabilities USPATFULL and USPAT2
NEWS 10	Nov 19	TOXCENTER(SM) - new toxicology file now available on STN
NEWS 11	Nov 29	COPPERLIT now available on STN
NEWS 12	Nov 29	DWPI revisions to NTIS and US Provisional Numbers
NEWS 13	Nov 30	Files VETU and VETB to have open access
NEWS 14	Dec 10	WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
NEWS 15	Dec 10	DGENE BLAST Homology Search
NEWS 16	Dec 17	WELDASEARCH now available on STN
NEWS 17	Dec 17	STANDARDS now available on STN
NEWS 18	Dec 17	New fields for DPCI
NEWS 19	Dec 19	CAS Roles modified
NEWS 20	Dec 19	1907-1946 data and page images added to CA and CAplus
NEWS 21	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 22	Jan 25	Searching with the P indicator for Preparations
NEWS 23	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS 24	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 25	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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 NEWS  2  Sep 17  IMSworld Pharmaceutical Company Directory name change
                  to PHARMASEARCH
 NEWS  3  Oct 09  Korean abstracts now included in Derwent World Patents
                  Index
 NEWS  4  Oct 09  Number of Derwent World Patents Index updates increased
 NEWS  5  Oct 15  Calculated properties now in the REGISTRY/ZREGISTRY File
 NEWS  6  Oct 22  Over 1 million reactions added to CASREACT
 NEWS  7  Oct 22  DGENE GETSIM has been improved
 NEWS  8  Oct 29  AAASD no longer available
 NEWS  9  Nov 19  New Search Capabilities  USPATFULL and USPAT2
 NEWS 10  Nov 19  TOXCENTER(SM) - new toxicology file now available on STN
 NEWS 11  Nov 29  COPPERLIT now available on STN
 NEWS 12  Nov 29  DWPI revisions to NTIS and US Provisional Numbers
 NEWS 13  Nov 30  Files VETU and VETB to have open access
 NEWS 14  Dec 10  WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
 NEWS 15  Dec 10  DGENE BLAST Homology Search
 NEWS 16  Dec 17  WELDASEARCH now available on STN
 NEWS 17  Dec 17  STANDARDS now available on STN
 NEWS 18  Dec 17  New fields for DPCI
 NEWS 19  Dec 19  CAS Roles modified
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 NEWS 21  Jan 25  BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS 22  Jan 25  Searching with the P indicator for Preparations
 NEWS 23  Jan 29  FSTA has been reloaded and moves to weekly updates
 NEWS 24  Feb 01  DKILIT now produced by FIZ Karlsruhe and has a new update
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 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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=> s Lamb J?/au or Dallman M?/au or Hoyne G?/au
L2         4132 LAMB J?/AU OR DALLMAN M?/AU OR HOYNE G?/AU

=> s l2 and notch
L3           28 L2 AND NOTCH

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PROCESSING COMPLETED FOR L3
L4 13 DUP REM L3 (15 DUPLICATES REMOVED)

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L4 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:123354 CAPLUS
TITLE: Assay
INVENTOR(S): **Lamb, Jonathan Robert; Hoyne, Gerard Francis; Dallman, Margaret Jane;** Champion, Brian Robert
PATENT ASSIGNEE(S): Lorantis Limited, UK
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012890	A2	20020214	WO 2001-GB3503	20010803

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-19242 A 20000804
AB A method for monitoring the immune system comprising monitoring the **Notch** signalling pathway.

L4 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:380426 CAPLUS
DOCUMENT NUMBER: 135:9978
TITLE: Immunotherapy with genetically engineered tumor-infiltrating lymphocytes
INVENTOR(S): **Lamb, Jonathan Robert; Hoyne, Gerard Francis**
PATENT ASSIGNEE(S): Lorantis Ltd., UK
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001035990	A2	20010525	WO 2000-GB4391	20001117

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-27328 A 19991118
AB A method is provided for enhancing the reactivity of a T cell toward a tumor cell which method comprises: (a) isolating a T cell which is a tumor-infiltrating lymphocyte (TIL) from a patient having said tumor cell present in their body; (b) introducing a nucleic acid sequence into the TIL, which sequence is capable of inhibiting or preventing expression of an endogenous **Notch** ligand in the TIL; and (c) re-introducing the transfected TIL into the patient; wherein the T cell comprises a T cell receptor specific for a tumor antigen expressed by the tumor cell.

L4 ANSWER 3 OF 13 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001677038 MEDLINE
DOCUMENT NUMBER: 21579863 PubMed ID: 11722637
TITLE: **Notch** signalling in the regulation of peripheral immunity.
AUTHOR: **Hoyne G F; Dallman M J;** Champion B R; **Lamb J R**
CORPORATE SOURCE: Immunobiology Group, Department of Pathology, Respiratory Medicine Unit, MRC Centre of Inflammation Research, University of Edinburgh, Edinburgh, UK.. g.hoyne@ed.ac.uk
SOURCE: IMMUNOLOGICAL REVIEWS, (2001 Aug) 182 215-27. Ref: 81
Journal code: 7702118. ISSN: 0105-2896.
PUB. COUNTRY: Denmark
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20011128
Last Updated on STN: 20020209
Entered Medline: 20020208
AB **Notch** signalling plays a critical role in embryogenesis, influencing the differentiation and growth of a variety of cell types across the species. In the mammalian immune system, **Notch** signalling operates at various levels; it controls the differentiation of haematopoietic stem cells and directs the early development of the T and B-cell lineages. It is also involved in the maturation of both CD4+ and CD8+ T cells in the thymus. The biological activities of this pathway extend beyond lymphocyte ontogeny; recent evidence has shown that it also contributes to the regulation of the peripheral immune system through its ability to influence cell survival and growth. In fulfilling this function, **Notch** signalling appears to act in conjunction with defined immunological signals such as cytokines, T-cell antigen receptor and co-stimulatory receptor-mediated signalling. In this review we discuss the potential of the **Notch** signalling pathway in the maintenance of homeostasis within the immune system affecting both peripheral tolerance and the negative feedback controlling productive immunity. The therapeutic manipulation of this pathway is likely to have broad application in a range of immunologically based diseases.

L4 ANSWER 4 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:178247 BIOSIS
DOCUMENT NUMBER: PREV200100178247
TITLE: Regulatory T cells: A role for **notch** signalling.
AUTHOR(S): **Lamb, J. (1); Dallman, M. J. (1); Hoyne, G. F. (1)**
CORPORATE SOURCE: (1) University of Edinburgh and Imperial College of Science, Technology and Medicine, London UK
SOURCE: Clinical and Experimental Allergy, (January, 2001) Vol. 31, No. 1, pp. 165. print.
Meeting Info.: Annual Meeting of the British Society for Allergy and Clinical Immunology Nottingham, England August 02-03, 2000 British Society for Allergy and Clinical Immunology
. ISSN: 0954-7894.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L4 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:421290 CAPLUS
DOCUMENT NUMBER: 133:72935
TITLE: Methods of immunosuppression
INVENTOR(S): **Lamb, Jonathan Robert; Dallman, Margaret Jane; Hoyne, Gerard Francis**
PATENT ASSIGNEE(S): Lorantis Ltd., UK
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000036089	A2	20000622	WO 1999-GB4233	19991215
WO 2000036089	A3	20001026		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1141243	A2	20011010	EP 1999-961206	19991215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001048930	A1	20011206	US 2001-870902	20010531

PRIORITY APPLN. INFO.: GB 1998-27604 A 19981215
WO 1999-GB4233 W 19991215

AB A method for producing a T cell having tolerance to an allergen or antigen which method comprises incubating the T cell with an antigen presenting cell (APC) in the presence of (i) a compn. capable of upregulating expression of an endogenous **Notch** ligand in the APC and (ii) the allergen or antigen is provided. The **Notch** or **Notch** ligand-upregulating compn. comprises a polypeptide selected from Noggin, Chordin, Follistatin, Xnr3, FGF or deriv.; and an immunosuppressive cytokine selected from IL-4, IL-10, IL-13, TGF-.beta. and FLT3.

L4 ANSWER 6 OF 13 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000404250 MEDLINE
DOCUMENT NUMBER: 20387636 PubMed ID: 10929049
TITLE: T-cell regulation of peripheral tolerance and immunity: the potential role for **Notch** signalling.
AUTHOR: **Hoyne G F; Dallman M J; Lamb J R**
CORPORATE SOURCE: Immunobiology Group, MRC Centre for Inflammation Research and the Respiratory Medicine Unit, University of Edinburgh, Teviot Place, Edinburgh, UK.
SOURCE: IMMUNOLOGY, (2000 Jul) 100 (3) 281-8. Ref: 36
Journal code: GH7; 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000901
Last Updated on STN: 20000901
Entered Medline: 20000821

AB Recognition of antigen by T cells in the periphery may lead either to the generation of productive immunity or the induction of tolerance. These two functional outcomes are a consequence of distinct pathways of T-cell differentiation. T cells are selected to become regulatory cells and their function is to maintain homeostasis with the immune system. In this review we discuss the cell-fate decisions that T cells might make allowing them to promote immunity or induce tolerance in the context of the role that **Notch** signalling may play in this process.

L4 ANSWER 7 OF 13 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2000120669 MEDLINE
DOCUMENT NUMBER: 20120669 PubMed ID: 10653853
TITLE: Serratel-induced **notch** signalling regulates the decision between immunity and tolerance made by peripheral CD4(+) T cells.
AUTHOR: **Hoyne G F**; Le Roux I; Corsin-Jimenez M; Tan K; Dunne J; Forsyth L M; **Dallman M J**; Owen M J; Ish-Horowicz D; **Lamb J R**
CORPORATE SOURCE: Respiratory Medicine Unit, University of Edinburgh Medical School, Teviot Place, Edinburgh EH8 9AG, UK.
SOURCE: INTERNATIONAL IMMUNOLOGY, (2000 Feb) 12 (2) 177-85.
Journal code: AY5; 8916182. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000505
Last Updated on STN: 20000505

Entered Medline: 20000424

AB Signals derived from antigen-presenting cells (APC) influence the functional differentiation of CD4(+) T cells. We report here that Serrate1 (Jagged1), a ligand for the Notch1 receptor, may contribute to the differentiation of peripheral CD4(+) T cells into either helper or regulatory cells. Our findings demonstrate that antigen presented by murine APC overexpressing human Serrate1 induces naive peripheral CD4(+) T cells to become regulatory cells. These cells can inhibit primary and secondary immune responses, and transfer antigen-specific tolerance to recipient mice. Our results show that **Notch** signalling may help explain 'linked' suppression in peripheral tolerance, whereby tolerance induced to one epitope encompasses all epitopes on that antigen during the course of an immune response.

L4 ANSWER 8 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:82870 BIOSIS
DOCUMENT NUMBER: PREV200100082870
TITLE: Use of conditional transgenic mice to study the role of **Notch** signaling in T cells.
AUTHOR(S): Tan, Karen (1); **Lamb, Jonathan R. (1)**; **Hoyne, Gerard F. (1)**
CORPORATE SOURCE: (1) Immunobiology Group, MRC Centre for Inflammation Research, University of Edinburgh Medical School, Teviot Place, Edinburgh, EH8 9AG UK
SOURCE: Immunology, (December, 2000) Vol. 101, No. Supplement 1, pp. 20. print.
Meeting Info.: Annual Congress of the British Society for Immunology Harrogate, UK December 05-08, 2000 British Society for Immunology
. ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L4 ANSWER 9 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:82827 BIOSIS
DOCUMENT NUMBER: PREV200100082827
TITLE: Role of the jagged/**notch** gene family in T-cell activation versus anergy.
AUTHOR(S): Ponchel, Frederique (1); Ali, Manir (1); Verhoef, Adrienne (1); **Lamb, Jonathan (1)**; Isaacs, John (1)
CORPORATE SOURCE: (1) Molecular Medicine Unit, University of Leeds, Leeds UK
SOURCE: Immunology, (December, 2000) Vol. 101, No. Supplement 1, pp. 8. print.
Meeting Info.: Annual Congress of the British Society for Immunology Harrogate, UK December 05-08, 2000 British Society for Immunology
. ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L4 ANSWER 10 OF 13 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1999242412 MEDLINE
DOCUMENT NUMBER: 99242412 PubMed ID: 10224357
TITLE: Linked suppression in peripheral T cell tolerance to the house dust mite derived allergen Der p 1.
AUTHOR: **Hoyne G F; Dallman M J; Lamb J R**
CORPORATE SOURCE: Respiratory Medicine Unit, Edinburgh University Medical School, Edinburgh, UK.
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1999 Feb-Apr) 118 (2-4) 122-4.
Journal code: BJ7; 9211652. ISSN: 1018-2438.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990618
Last Updated on STN: 19990618
Entered Medline: 19990610

AB BACKGROUND: Peripheral tolerance is required to maintain balance within the immune system. A feature of peripheral tolerance is linked suppression, in which tolerance induced to a single T cell epitope inhibits the response to all epitopes in the same protein. It is suggested that this phenomenon is mediated by regulatory T cells through either the activity of immunopressive cytokines or direct cell contact. In previous experiments we failed to detect inhibitory cytokines when T cells from mice rendered tolerant by intranasal delivery of the immunodominant peptide of Der p 1 (p 1, 110-131) were restimulated with peptide in vitro. Therefore, the aim of this study was to determine if cognate interactions between T cells mediated by **Notch**/Delta signaling induce and maintain peripheral T cell tolerance. METHODS: Using in situ hybridization and viral mediated gene transfer, the expression and function of Delta1 were investigated in a murine model of T cell tolerance to Der p 1 in vivo. RESULTS: Delta1 expression is increased on peripheral T cells during the induction of tolerance with high-dose peptide delivered intranasally and when tolerant animals are rechallenged under immunogenic conditions. Peptide p 1, 110-131-specific CD4+ T cells transfected with Delta1 inhibited the response of antigen-primed T cells and induced linked suppression. CONCLUSIONS: High-dose peptide delivered intranasally induces transient expression of Delta 1 on inhibitory CD4+ T cells. Ligation of the Notch1 receptor on neighbouring T cells by Delta1+ regulatory T cells inhibits clonal expansion of the former and mediates linked suppression.

L4 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:324898 CAPLUS
DOCUMENT NUMBER: 128:320575
TITLE: Controlling abnormal immune responses by modulation of the interactions between members of the **Notch** family of proteins
INVENTOR(S): **Lamb, Jonathan Robert; Dallman, Margaret Jane; Hoyne, Gerald Francis**
PATENT ASSIGNEE(S): Imperial College of Science Technology & Medicine, UK; Lamb, Jonathan Robert; Dallman, Margaret Jane; Hoyne, Gerald Francis
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9820142	A1	19980514	WO 1997-GB3058	19971106
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9748765	A1	19980529	AU 1997-48765	19971106
AU 736361	B2	20010726		
GB 2335194	A1	19990915	GB 1999-10276	19971106
GB 2335194	B2	20010425		
EP 942998	A1	19990922	EP 1997-911353	19971106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1242802	A	20000126	CN 1997-181159	19971106
GB 2353094	A1	20010214	GB 2000-23691	19971106
GB 2353094	B2	20010613		
JP 2001504331	T2	20010403	JP 1998-521150	19971106
NO 9902196	A	19990705	NO 1999-2196	19990505

PRIORITY APPLN. INFO.:	GB 1996-23236	A	19961107
	GB 1997-15674	A	19970724
	GB 1997-19350	A	19970911
	GB 1999-10276	A3	19971106
	WO 1997-GB3058	W	19971106

AB Methods of modifying the interaction of components such as T-cells, T-cell-antigen presenting cells (APC) and between pathogenic organisms and immunocompetent cells of a host using members of the **Notch** protein family and their ligands are described. Hybridoma cells expressing the gene for Delta protein were shown to prevent antigen-primed lymphocytes from proliferating upon exposure to the priming antigen. Dendritic cells expressing the Serrate gene prevented the antigen priming of T cells. The use T cell hybridomas expressing the Delta gene to inhibit the development of immunity to the Der p 1 is demonstrated.

L4 ANSWER 12 OF 13 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1998384211 MEDLINE
DOCUMENT NUMBER: 98384211 PubMed ID: 9716576
TITLE: Stromal expression of Jagged 1 promotes colony formation by fetal hematopoietic progenitor cells.
AUTHOR: Jones P; May G; Healy L; Brown J; **Hoyne G**; Delassus S; Enver T
CORPORATE SOURCE: Section of Gene Function and Regulation & Leukaemia Research Fund Centre, Chester Beatty Laboratories, Institute of Cancer Research, London, UK.
SOURCE: BLOOD, (1998 Sep 1) 92 (5) 1505-11.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 20000303
Entered Medline: 19980910

AB The **Notch** signaling system regulates proliferation and differentiation in many tissues. **Notch** is a transmembrane receptor activated by ligands expressed on adjacent cells. Hematopoietic stem cells and early progenitors express **Notch**, making the stromal cells which form cell-cell contacts with progenitor cells candidate ligand-presenting cells in the hematopoietic microenvironment. Therefore, we examined primary stromal cell cultures for expression of **Notch** ligands. Using reverse transcription-polymerase chain reaction, in situ hybridization, immunohistochemistry, and Western blotting, we demonstrate expression of Jagged 1 in primary stromal cultures. To investigate if the stromal expression of Jagged 1 has functional effects on hematopoietic progenitors, we cultured CD34(+), c-kit+ hematopoietic progenitor cells derived from the aorto gonadal mesonephros region of day 11 mouse embryos on the Jagged 1(-) stromal cell line S17 and on S17 cells engineered to express Jagged 1. The presence of Jagged 1 increased the number of colonies formed in subsequent methylcellulose culture fourfold. Larger increases in colony numbers were observed under the same culture conditions with CD34(+), c-kit+ hematopoietic progenitor cells derived from d11 fetal liver. These results obtained in vitro table Jagged 1 as a candidate regulator of stem cell fate in the context of stromal microenvironments in vivo.

L4 ANSWER 13 OF 13 CAPLUS
ACCESSION NUMBER: 1947:9010 CAPLUS
DOCUMENT NUMBER: 41:9010
ORIGINAL REFERENCE NO.: 41:1875c-e
TITLE: Impact strength and flexural properties of laminated plastics at high and low temperatures
AUTHOR(S): **Lamb, J. J.**; Albrecht, Isabelle; Axilrod, B. M.
CORPORATE SOURCE: Natl. Bur. Standards, Washington, DC
SOURCE: Natl. Advisory Comm. Aeronautics, Tech. Note (1946), No. 1054, 30 pp.
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The materials investigated were unsatd. polyester laminates reinforced with glass fabric (I), and phenolic laminates reinforced with asbestos fabric (II), high-strength paper (III), rayon fabric (IV), and cotton fabric (V). V was studied in both the high- and low-pressure types. The Izod-impact strength at 77.degree.F. was 4 to 7 ft.-lb. per in. of **notch** for II, III, and V; I and IV had strengths of 31 and 17 ft.-lb., resp. Impact strength of I decreased to about 70% of its -70.degree. value at 200.degree.F.; II, III, and IV showed little change with temp. V approx. doubled in strength between -70 and 200.degree.F. Outstanding flexural properties were shown by I and III, but on the basis of sp. strengths, III and IV were superior to the others. Flexural properties increased for all materials at low temp., and decreased at high temp. except for II, which showed no change at high temp. It was emphasized that change in flexural properties at high temp. may be a function of humidity and further cure as well as temp. per se.

=> s admist? (P) (notch or serrate or ser or delta)

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L5          1 ADMIST? (P) (NOTCH OR SERRATE OR SER OR DELTA)

=> dis l5

L5   ANSWER 1 OF 1  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN   1989:402440  BIOSIS
DN   BA88:71865
TI   FULMINANT LIVER FAILURE.
AU   GALLARDO M; NOFUENTES G; GOMEZ J L; RODRIQUEZ F; CORDON A; GIL A; IBANEZ
     J; GARIJO A
CS   HOSP. REG. "CARLOS HAYA". MALAGA, SERV. MED. INTENSIVA.
SO   REV ESP ENFERM APAR DIG, (1989) 75 (4), 359-365.
     CODEN: READBN. ISSN: 0034-9437.
FS   BA; OLD
LA   Spanish


=> dis l5 1 ibib abs kwic

L5   ANSWER 1 OF 1  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER:   1989:402440  BIOSIS
DOCUMENT NUMBER:    BA88:71865
TITLE:              FULMINANT LIVER FAILURE.
AUTHOR(S):          GALLARDO M; NOFUENTES G; GOMEZ J L; RODRIQUEZ F; CORDON A;
                    GIL A; IBANEZ J; GARIJO A
CORPORATE SOURCE:   HOSP. REG. "CARLOS HAYA". MALAGA, SERV. MED. INTENSIVA.
SOURCE:             REV ESP ENFERM APAR DIG, (1989) 75 (4), 359-365.
                    CODEN: READBN. ISSN: 0034-9437.
FILE SEGMENT:       BA; OLD
LANGUAGE:           Spanish
AB   We analyze the patients admistted to the Intensive Medicine
     Department of the .mchlt.Carlos Haya.mchgt. Regional Hospital of Malaga
     (Spain) with a diagnosis of fulminant liver failure (IHF) between 1980 and
     October 1986. There were 7 patients, 6 women and one man: 5 had a picture
     of fulminant hepatitis, one pregnant female had fatty liver, and the man
     had fulminant hepatitis due to accidental inhalation of carbon
     tetrachloride. The average age of the group was 32 years. Six patients (85
     %) died; their average stay was 4.6 days, ranging from 10 hours to 7 days.
     The woman who survived spent 17 days in the unit. Postmortem studies were
     made in 4 patients. In the pregnant patient with fatty liver, 36 weeks
     gestation. a cesarean was performed and a live female fetus of 2,720 g.
     weight was extracted. Some pathogenic aspects of the disease are
     discussed, such as the incidence of superinfection by other viruses (
     delta virus), the influence of immunological factors on the
     development of fulminant liver failure, morphological findings,
     therapeutic results and the need for multicenter studies.
AB   We analyze the patients admistted to the Intensive Medicine
     Department of the .mchlt.Carlos Haya.mchgt. Regional Hospital of Malaga
     (Spain) with a diagnosis of fulminant liver.  .  .  weight was extracted.
     Some pathogenic aspects of the disease are discussed, such as the
     incidence of superinfection by other viruses (delta virus), the
     influence of immunological factors on the development of fulminant liver
     failure, morphological findings, therapeutic results and the need.  .  .


=> s administ? (P) (notch or serrate or ser or delta)
L6       22582 ADMINIST? (P) (NOTCH OR SERRATE OR SER OR DELTA)

=> s administ? (P) (serrate or ser or delta)
L7       22425 ADMINIST? (P) (SERRATE OR SER OR DELTA)

=> s ( administ? (P) (serrate or or ser or delta)) and notch
MISSING TERM 'OR OR'
The search profile that was entered contains a logical
operator followed immediately by another operator.

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L8           4 (ADMINIST? (P) (SERRATE OR SER OR DELTA)) AND NOTCH

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9           3 DUP REM L8 (1 DUPLICATE REMOVED)

=> dis l9 1-3 ibib abs kwic

L9   ANSWER 1 OF 3     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:   91140959     MEDLINE
DOCUMENT NUMBER:    91140959   PubMed ID: 2287123
TITLE:              The Wolff-Parkinson-White syndrome in a Holstein-Friesian
                    cow.
AUTHOR:             Endo Y; Tajima M; Kurosawa T; Takahashi K; Sonoda M
CORPORATE SOURCE:   Department of Veterinary Internal Medicine, Rakuno Gakuen
                    University, Ebetsu, Japan.
SOURCE:             NIPPON JUIGAKU ZASSHI. JAPANESE JOURNAL OF VETERINARY
                    SCIENCE, (1990 Dec) 52 (6) 1155-61.
                    Journal code: KRJ; 0057113. ISSN: 0021-5295.
PUB. COUNTRY:       Japan
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199103
ENTRY DATE:         Entered STN: 19910412
                    Last Updated on STN: 19910412
                    Entered Medline: 19910328
AB   A case of Wolff-Parkinson-White (WPW) syndrome in a Holstein-Freisian cow
     aged 10-year-old was examined in detail. In electrocardiogram (ECG), the
     P-wave was the same configuration in both the normal and abnormal ECG. The
     PR-interval shortened from 0.2 to 0.1 second and the duration of the
     QRS-complex prolonged from 0.1 to 0.12 second compared with normal ECG.
     The delta wave, characterized in WPW syndrome, could not be
     recognized. In echocardiogram, notches were recognized at the
     early stage of ventricular contraction in the interventricular septum.
     This cow was, therefore, diagnosed as type B WPW syndrome. The abnormal
     ECG disappeared by the administration of procainamide. It was
     strongly indicated that the ventricular contraction showing abnormal ECG
     was generated only by the stimulation through an accessory pathway in this
     cow.
AB   .  .  .  to 0.1 second and the duration of the QRS-complex prolonged from
     0.1 to 0.12 second compared with normal ECG. The delta wave,
     characterized in WPW syndrome, could not be recognized. In echocardiogram,
     notches were recognized at the early stage of ventricular
     contraction in the interventricular septum. This cow was, therefore,
     diagnosed as type B WPW syndrome. The abnormal ECG disappeared by the
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administration of procainamide. It was strongly indicated that the ventricular contraction showing abnormal ECG was generated only by the stimulation through. . .

L9 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1987:445325 BIOSIS
DOCUMENT NUMBER: BA84:101163
TITLE: A CLINICAL STUDY OF THE SECOND COMPONENT OF LEFT VENTRICULAR SYSTOLIC PRESSURE.
AUTHOR(S): TAKAZAWA K
CORPORATE SOURCE: DEP. INTERN. MED., TOKYO MED. COLL.
SOURCE: J TOKYO MED COLL, (1987) 45 (2), 256-270.
CODEN: TIDZAH. ISSN: 0040-8905.
FILE SEGMENT: BA; OLD
LANGUAGE: Japanese

AB Arterial and left ventricular systolic pressure are divided into two components by the anacrotic **notch**. The first component is mainly caused by the left ventricular ejection and the second component by the peripheral reflection wave. The increase in the second component of the left ventricular pressure comes after the peak of the left ventricular ejection and is probably a part of excessive left ventricular afterload. The purpose of this study was to compare the second component of the left ventricular pressure and investigate the changes after an intravenous injection of angiotensin and a sublingual **administration** of nitroglycerin. Forty-nine patients, 18 with myocardial infarction (MI group), 20 with angina pectoris (AP group) and 11 others (Ot group) were studied. The pressure in the left ventricle and at the base of the ascending aorta were measured by means of a micromanometer-tipped catheter (Miller-PC-484A) in the subjects' normal conditions and after an intravenous injection of 2.5 .mu.g angiotensin and a sublingual **administration** of 0.3 mg nitroglycerin. Aortic reflection wave ratio (AoRWR) and left ventricular reflection wave ratio (LVRWR) were expressed as follows: (AoRWR) = (late peak aortic systolic pressure-pressure at anacrotic **notch**)/(pulse pressure) .times. 100 (%); (LVRWR) = (late peak left ventricular systolic pressure - left ventricular pressure at anacrotic **notch**)/(late peak left ventricular systolic pressure) .times. 100 (%). There was no statistical difference in the mean ages of patients in the three groups and the mean systolic and diastolic aortic pressures of them. AoRWR was 40.7 .+-. 11.0 (mean .+-. 1 SD) % in the MI group, 36.6 .+-. 9.6% in the AP group and 30.3 .+-. 11.0% in the Ot group. LVRWR was 16.7 .+-. 5.7% in the MI group, 13.3 .+-. 6.3% in the AP group and 9.4 .+-. 5.6% in the Ot group. LVRWR and AoRWR were higher in the ischemic heart disease groups than in the Ot group. LVRWR (Y) and AoRWR (X) were directly proportional, Y = 0.488X - 4.3 ($r = 0.83$, $p < 0.001$), as were the changes after angiotensin loading and nitroglycerin. .**DELTA**.LVEDP/.**DELTA**.LVRWR was high in the MI patients who received angiotensin. Nitroglycerin produced a marked decrease in LVRWR without an accompanying decrease in the aortic diastolic pressure. The ratio of the second component to the increase in the left ventricular pressure is considered to be a useful index of the excessive left ventricular afterload.

AB Arterial and left ventricular systolic pressure are divided into two components by the anacrotic **notch**. The first component is mainly caused by the left ventricular ejection and the second component by the peripheral reflection wave.. . . second component of the left ventricular pressure and investigate the changes after an intravenous injection of angiotensin and a sublingual **administration** of nitroglycerin. Forty-nine patients, 18 with myocardial infarction (MI group), 20 with angina pectoris (AP group) and 11 others (Ot. . . micromanometer-tipped catheter (Miller-PC-484A) in the subjects' normal conditions and after an intravenous injection of 2.5 .mu.g angiotensin and a sublingual **administration** of 0.3 mg nitroglycerin. Aortic reflection wave ratio (AoRWR) and left ventricular reflection wave ratio (LVRWR) were expressed as follows: (AoRWR) = (late peak aortic systolic pressure-pressure at anacrotic **notch**)/(pulse pressure) .times. 100 (%); (LVRWR) = (late peak left ventricular systolic pressure - left ventricular pressure at anacrotic **notch**)/(late peak left ventricular systolic pressure) .times. 100 (%). There was no statistical difference in the mean ages of patients in. . . Y = 0.488X - 4.3 ($r = 0.83$, $p < 0.001$), as were the changes after angiotensin loading and nitroglycerin. .**DELTA**.LVEDP/.**DELTA**.LVRWR was high in the MI patients who received angiotensin. Nitroglycerin produced a marked decrease in LVRWR without an accompanying decrease. . .

L9 ANSWER 3 OF 3 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 77031163 EMBASE
DOCUMENT NUMBER: 1977031163
TITLE: [An unusual electroclinical event during one case of L Dopa treatment).
A PROPOS D'UN ASPECT ELECTROCLINIQUE PARTICULIER OBSERVE DANS LE COURS D'UN TRAITEMENT A LA L DOPA.
AUTHOR: Lavaivre M.; Sainty J.M.; Conte Devolx J.; et al.
CORPORATE SOURCE: Serv. EEG, Secteur Sud, CHU, Marseille, France
SOURCE: Revue d'E.E.G. et de Neuro-Physiologie Clinique, (1975) 5/4 (395-398).
CODEN: RENCBH
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
030 Pharmacology
LANGUAGE: French

AB A woman of 62 had suffered from Parkinson's disease from the age of 40 and had been treated with L Dopa in a dosage of 4 g. daily. On 3 occasions during this treatment she had developed more or less severe cardiorespiratory distress. In the most alarming attack, with cyanosis, polypnoea, struggling for breath, and cardiovascular collapse, necessitating intubation with the **administration** of corticoids and tranquillizers, the EEG showed, besides a dysrhythmia some sinusoidal **delta** waves, with steep gradients and an amplitude up to 100-150 microvolts with **notches** on the crest. These abnormalities appear in bifrontal hypersynchronised bursts at 2-2.5 cycles per sec. The visual reaction of arrest is present for the alpha rhythm, to a degree which declines for the slow activities. After 24 hours, the EEG returns to normal while the calm patient once more shows a Parkinsonian tremor. The authors discuss the relationship between cardiorespiratory disorders and EEG anomalies as shown in their patient, with the signs of intolerance to L Dopa already described in the literature. (Isch - Strasbourg)

AB . . . cardiorespiratory distress. In the most alarming attack, with cyanosis, polypnoea, struggling for breath, and cardiovascular collapse, necessitating intubation with the **administration** of corticoids and tranquillizers, the EEG showed, besides a dysrhythmia some sinusoidal **delta** waves, with steep gradients and an amplitude up to 100-150 microvolts with **notches** on the crest. These abnormalities appear

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     in bifrontal hypersynchronised bursts at 2-2.5 cycles per sec. The visual
     reaction of arrest.  .  .


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     (FILE 'HOME' ENTERED AT 17:46:43 ON 23 FEB 2002)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 17:46:59 ON 23 FEB 2002
L1          1390 S LAMBJ?/AU OR DALLMAN M?/AU OR HOYNE G?/AU
L2          4132 S LAMB J?/AU OR DALLMAN M?/AU OR HOYNE G?/AU
L3            28 S L2 AND NOTCH
L4            13 DUP REM L3 (15 DUPLICATES REMOVED)
L5             1 S ADMIST? (P) (NOTCH OR SERRATE OR SER OR DELTA)
L6         22582 S ADMINIST? (P) (NOTCH OR SERRATE OR SER OR DELTA)
L7         22425 S ADMINIST? (P) (SERRATE OR SER OR DELTA)
L8             4 S ( ADMINIST? (P) (SERRATE OR SER OR DELTA)) AND NOTCH
L9             3 DUP REM L8 (1 DUPLICATE REMOVED)

=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    75.45      75.60

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -3.10      -3.10

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Sep 17  IMSworld Pharmaceutical Company Directory name change
                  to PHARMASEARCH
 NEWS  3  Oct 09  Korean abstracts now included in Derwent World Patents
                  Index
 NEWS  4  Oct 09  Number of Derwent World Patents Index updates increased
 NEWS  5  Oct 15  Calculated properties now in the REGISTRY/ZREGISTRY File
 NEWS  6  Oct 22  Over 1 million reactions added to CASREACT
 NEWS  7  Oct 22  DGENE GETSIM has been improved
 NEWS  8  Oct 29  AAASD no longer available
 NEWS  9  Nov 19  New Search Capabilities  USPATFULL and USPAT2
 NEWS 10  Nov 19  TOXCENTER(SM) - new toxicology file now available on STN
 NEWS 11  Nov 29  COPPERLIT now available on STN
 NEWS 12  Nov 29  DWPI revisions to NTIS and US Provisional Numbers
 NEWS 13  Nov 30  Files VETU and VETB to have open access
 NEWS 14  Dec 10  WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
 NEWS 15  Dec 10  DGENE BLAST Homology Search
 NEWS 16  Dec 17  WELDASEARCH now available on STN
 NEWS 17  Dec 17  STANDARDS now available on STN
 NEWS 18  Dec 17  New fields for DPCI
 NEWS 19  Dec 19  CAS Roles modified
 NEWS 20  Dec 19  1907-1946 data and page images added to CA and CAplus
 NEWS 21  Jan 25  BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS 22  Jan 25  Searching with the P indicator for Preparations
 NEWS 23  Jan 29  FSTA has been reloaded and moves to weekly updates
 NEWS 24  Feb 01  DKILIT now produced by FIZ Karlsruhe and has a new update
                  frequency
 NEWS 25  Feb 19  Access via Tymnet and SprintNet Eliminated Effective 3/31/02

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

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=> file medline caplus embase biosis
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.15       0.15

FILE 'MEDLINE' ENTERED AT 11:19:07 ON 24 FEB 2002

FILE 'CAPLUS' ENTERED AT 11:19:07 ON 24 FEB 2002
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FILE 'EMBASE' ENTERED AT 11:19:07 ON 24 FEB 2002
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FILE 'BIOSIS' ENTERED AT 11:19:07 ON 24 FEB 2002

=> s jagged (P) notch
L1 240 JAGGED (P) NOTCH

=> s (administ? (10N) jagged) (P) notch
L2 0 (ADMINIST? (10N) JAGGED) (P) NOTCH

=> s (administ? (10N) jagged)
L3 0 (ADMINIST? (10N) JAGGED)

=> s (administ? (P) jagged)
L4 12 (ADMINIST? (P) JAGGED)

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5 6 DUP REM L4 (6 DUPLICATES REMOVED)

=> dis l5 1-6 kwic

L5 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2002 ACS
AB . . . g were used. Tight junctions were found impermeable to microperoxidase in the control gland. However, at 3 min after carbachol **administration**, tight junctions become permeable. In control acini, the tight junction protein, ZO-1 was highly concd. at the luminal site of. . . .beta.-catenin and vinculin. Cytoplasmic aggregates of F-actin were seen and were colocalized with both ZO-1 and vinculin. In the carbachol **administered** gland, expression of ZO-1 was expanded, not only to the tight junctional region, but also lateral membranes. The staining pattern of E-cadherin was not **jagged** or discontinuous as was the pattern obsd. for vinculin. Results indicate that secretory stimulation leads to alteration in the architecture. . .

L5 ANSWER 2 OF 6 MEDLINE DUPLICATE 1
AB . . . . various indices of dysgraphia and constructional apraxia. Second, a series of 56 psychiatric inpatients with delirium as identified using electronic **administrative** data and clinical records was selected to evaluate sensitivity. RESULTS: Of the various indices of dysgraphia examined, only a global rating of writing quality and evidence of **jagged** or angled letter loops were informative clinical signs. The predictive value of constructional apraxia resembled the predictive value of the. . .

L5 ANSWER 3 OF 6 MEDLINE DUPLICATE 2
AB . . . . in serum concentrations is often observed after intermittent infusion of vancomycin at the usual dose of 30 mg/kg. This specific " **jagged**" pharmokinetic course with inadequate residual concentrations raises the problem of the efficacy of this time-dependent antibiotic. Studies in patients in general resuscitation units have shown the interest of vancomycin **administration** in continuous infusion. METHODS: We analyzed variations in serum concentrations of vancomycin during continuous infusion in 18 patients with burns. . . under 60) than in other patients. Impairment of renal function is a contra-indication of continuous infusion. CONCLUSION: This mode of **administration** has the advantage of ensuring greater efficacy by preventing fluctuations in serum concentrations.

L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2002 ACS
AB The hepatotoxicity of p-chloro-m-xylenol (I) was demonstrated in primary culture of rat hepatocytes. The **administration** of I at 5 .times. 10-4 M reduced cell viability to 32% at 2 h of exposure and killed most. . . h. In addn., the morphol. of the hepatocytes showed a no. of cytol. changes such as size and shape deformation, **jagged** plasma membranes and lysed cells. I was also interfered with the metabolic function of the hepatocytes. These findings suggest that. . .

L5 ANSWER 5 OF 6 MEDLINE DUPLICATE 3
AB . . . . fetal Rh disease) or intrapartum (one case with an acute episode of fetomaternal transfusion as possible cause, 2 after meperidine **administration** to the mother and 2 others without attributable causes). Characteristics of both SHR patterns and related clinical pictures are described. . . similar cases published elsewhere. The possible underlying mechanisms of SHR are discussed. Two different profiles of SHR patterns (smooth and **jagged** waveforms) are characterized and correlated with their most usual clinical backgrounds and prognostic significance. A classification of SHR into 2. . .

L5 ANSWER 6 OF 6 MEDLINE DUPLICATE 4
AB . . . . intermittent quality. A projective test was developed using cartoons to illustrate two situations in which children commonly experience pain, a self-**administered** hammer blow and a doctor-**administered** needle. Interviews were tape-recorded with 58 children in hospital outpatient clinics and school situations in Kindergarten and Grades 1 through 3 in Licking County, Ohio. Significantly more children perceived the pain of a needle as **jagged** rather than smooth, and the pain of a hammer blow as a continuous rather than on-and-off pain. A finding of. . .

=> dis his

(FILE 'HOME' ENTERED AT 11:18:57 ON 24 FEB 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 11:19:07 ON 24 FEB 2002
L1 240 S JAGGED (P) NOTCH
L2 0 S (ADMINIST? (10N) JAGGED) (P) NOTCH
L3 0 S (ADMINIST? (10N) JAGGED)
L4 12 S (ADMINIST? (P) JAGGED)
L5 6 DUP REM L4 (6 DUPLICATES REMOVED)

=> s l1 (P) ligand
L6 180 L1 (P) LIGAND

=> s l6 (P) (pharmaceut? or therap?)
L7 0 L6 (P) (PHARMACEUT? OR THERAP?)

=> dup rem l6
PROCESSING COMPLETED FOR L6
L8 76 DUP REM L6 (104 DUPLICATES REMOVED)

=> dis l8 1-20 kwic

L8 ANSWER 1 OF 76 MEDLINE DUPLICATE 1
AB We have previously demonstrated that the expression of the soluble extracellular domain of the transmembrane **ligand** for **Notch** receptors, **Jagged** 1 (sJ1), in NIH 3T3 cells results in the formation of a matrix-dependent chord-like phenotype, the loss of contact inhibition. . . . that the sJ1-mediated induction of Src activity and related phenotypes, including chord formation, may result from the inhibition of endogenous **Jagged** 1-mediated **Notch** signaling since it was not possible to detect an sJ1-dependent induction of CSL-dependent transcription in these cells. Interestingly, NIH 3T3 cells transfected with dominant-negative (but not constitutively active) mutants of either **Notch** 1 or **Notch** 2 displayed a similar Src-related phenotype as the sJ1 transfectants. These data suggest that the ability of sJ1 to mediate chord formation is Src-dependent and requires the repression of endogenous **Jagged** 1-mediated **Notch** signaling, which is tolerant to the destabilization of the actin cytoskeleton, a mediator of cell migration.

L8 ANSWER 2 OF 76 MEDLINE DUPLICATE 2
AB **Notch** proteins function as receptors for membrane-bound **ligands** (**Jagged** and Delta-like) to regulate cell-fate determination. We have investigated the role of **Notch** signaling in embryonic endothelium of the mouse by expressing an activated form of the Notch4 protein in vasculature under the. . . abnormal. Expression of an activated form of Notch4 in embryonic vasculature leads to abnormal vessel structure and patterning, implicating the **Notch** pathway in phases of vascular development associated with vessel patterning and remodeling.

L8 ANSWER 3 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
IT . . .
inner ear: development, sensory regions, sensory system; non-sensory epithelium; organ of Corti: sensory system; sensory epithelium
IT Chemicals & Biochemicals
Jagged 1: **Notch ligand**; **Notch**: signalling

L8 ANSWER 4 OF 76 MEDLINE DUPLICATE 3
AB . . . stages of T cell development in the thymus, yet the molecular basis of this specialization is largely unknown. Recently, the **Notch** family of transmembrane proteins has been implicated in thymocyte development. Such proteins interact with cell surface proteins of the Delta-like and **Jagged** families. It is known that **Notch ligands** are expressed intrathymically, and that **Notch** signaling is regulated by **Notch ligands** expressed on either the same or third-party cells. However, functional analysis of **Notch ligand** expression, and elucidation of the mechanism of **Notch ligand** signaling in thymocyte development, are unclear. Here, we find that **Notch ligand** expression in the thymus is compartmentalized, with MHC class II(+) thymic epithelium, but not thymocytes nor dendritic cells, expressing **Jagged**-1, **Jagged**-2 and Delta-like-1. We also provide evidence that contact with **Notch ligands** on thymic epithelium is necessary to activate and sustain **Notch** signaling in thymocytes, and that this can occur independently of positive selection induction. Our data suggest that **Notch ligand** expression by thymic epithelium may partly explain the specialization of these cells in supporting thymocyte development, by regulating **Notch** activation via an inductive signaling mechanism independently of signaling leading to positive selection.

L8 ANSWER 5 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AB. . . mechanisms of radial glia differentiation we studied the regulation of erbB receptor expression in these cells. We now show that **Notch** and its **ligands** are critical in these events. In the developing cerebellum Notch1 is expressed by Bergmann glia and granule cells express **Notch ligands**. Using neuron-glia co-cultures we show that granule cells induce **Notch** signaling in cerebellar astrocytes and also induce the expression of erbB2 receptors in glia as they do with BLBP, a radial glia protein. **Notch** signaling is necessary and sufficient for these effects, since contact with **Jagged**-expressing fibroblast or expression of an activated form of **Notch** lead to the same changes in glia as neuronal contact, and expression of a dominant-negative **Notch** in glia abolishes the effect of neuronal contact. In contrast, erbB receptor activation does not induce erbB2 or BLBP expression. Finally, blocking **Notch** signaling also blocks the ability of neurons to induce radial glia formation to the same extent as a DN-erbB receptor. Our results suggest that **Notch** signaling is an early step in the program of neuronal-induced radial glia differentiation, and that this is mediated by inducing. . .

L8 ANSWER 6 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AB **Notch** signaling is important in normal development and cell specification in many organisms. Jagged1, a **notch** receptor **ligand**, is present in developing liver and implicated in the abnormal development of the biliary tree in Alagille syndrome. In this. . . mesenchyme. In normal liver, Notch1-4 stained endothelial cells, additionally Notch2 and 3 also stained occasional biliary epithelial cells (BEC) and **Jagged** 1 colocalised with CK19 on BEC. In diseased tissue, Notch2 additionally stained stromal cells in portal tracts and cirrhotic fibrous. . .

L8 ANSWER 7 OF 76 MEDLINE DUPLICATE 4
AB **Notch** receptors are involved in a variety of cell-fate decisions that affect the development and function of many organs, including hematopoiesis and the immune system. There are four mammalian **Notch** receptors that have only partially overlapping functions despite sharing similar structures and **ligands**. The **ligands** for **Notch** are transmembrane proteins expressed on adjacent cells, including **Jagged** and Delta, and it is quite possible that signaling is bidirectional. A large **Notch** precursor protein is proteolytically cleaved to form the mature cell-surface receptor. **Ligand** binding induces additional proteolytic events followed by translocation of the intracellular domain to the nucleus. There, **Notch** interacts with transcription factors such as RBPJ kappa, activating transcription of basic helix-loop-helix genes such as HES1. These in turn regulate expression of tissue-specific transcription factors that influence lineage commitment and other events. In this review, the details of **Notch** signaling

will be discussed, with a focus on what is known about the role of **Notch** in hematopoiesis.

L8 ANSWER 8 OF 76 MEDLINE DUPLICATE 5
TI Requirement of **Notch** 1 and its **ligand jagged** 2 expressions for spermatogenesis in rat and human testes.

L8 ANSWER 9 OF 76 MEDLINE DUPLICATE 6
TI Differential effects of **Notch ligands** Delta-1 and **Jagged**-1 in human lymphoid differentiation.
AB **Notch** signaling is known to differentially affect the development of lymphoid B and T cell lineages, but it remains unclear whether such effects are specifically dependent on distinct **Notch ligands**. Using a cell coculture assay we observed that the **Notch ligand** Delta-1 completely inhibits the differentiation of human hematopoietic progenitors into the B cell lineage while promoting the emergence of cells with a phenotype of T cell/natural killer (NK) precursors. In contrast, **Jagged**-1 did not disturb either B or T cell/NK development. Furthermore, cells cultured in the presence of either Delta-1 or **Jagged**-1 can acquire a phenotype of NK cells, and Delta-1, but not **Jagged**-1, permits the emergence of a de novo cell population coexpressing CD4 and CD8. Our results thus indicate that distinct **Notch ligands** can mediate differential effects of **Notch** signaling and provide a useful system to further address cell-fate decision processes in lymphopoiesis.

L8 ANSWER 10 OF 76 MEDLINE DUPLICATE 7
AB Members of the **Notch** gene family have been shown to play an important role in the control of cell fate in many developmental systems. We hypothesized that the fate of the male germ line stem cells may also be mediated through the **Notch** signaling pathway. We therefore sought to determine whether the components of the **Notch** pathway are expressed in the mouse testis. Western blot analysis revealed the expression of three **Notch** receptors (**Notch** 1, **Notch** 2, and **Notch** 3), **Notch ligands** (**Jagged** 1, **Jagged** 2, and Delta 1), and presenilin 1 (PS1) in neonatal mouse testis. We then examined their cellular localization by immunohistochemical analysis of cocultures of spermatogonia and Sertoli cells. The 3 **Notch** receptors were found to be expressed in spermatogonia. Sertoli cells expressed only **Notch** 2 receptor. Among the **Notch ligands**, Delta 1 and **Jagged** 1 were localized exclusively in spermatogonia and Sertoli cells, respectively. PS1 was apparent in both spermatogonia and Sertoli cells. The presence of **Notch** receptors and **Notch ligands** in spermatogonia and Sertoli cells indicates that these cells are capable of responding to and eliciting **Notch** signaling during the process of spermatogenesis. Key words: Cell fate, delta, **jagged**, presenilin, spermatogenesis.

L8 ANSWER 11 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AB **Notch** signaling is an evolutionarily conserved mechanism, used to regulate cell fate decisions. Four **Notch** receptors have been identified in man (**Notch**-1 to -4), together with two **Notch ligand** families, Delta (Delta-1, -3 and -4) and Serrate/**Jagged** (**Jagged**-1 and -2). Using total RNA isolated from whole tissue, semi-quantitative RT-PCR was used to determine which **Notch** signaling components were expressed in the adult liver and whether their expression was perturbed in disease. Although no significant differences in the levels of expression for the **Notch** receptors was seen, the expression of **Jagged**-1 was found to be elevated in primary biliary cirrhosis and primary sclerosing cholangitis liver. **Jagged**-2 and Delta-1 gene expression was not detectable in normal or diseased liver. To localise **Notch** receptor and **ligand** expression, purified cell types were isolated from normal and diseased liver. Semi-quantitative RT-PCR using RNA isolated from cells, together with immunostaining of liver sections revealed that **Jagged**-1 expression was present in hepatocytes, bile ducts and the vasculature. The distribution of **Notch**-1 and -4 was similar, with both receptors detectable at low levels in hepatocytes and the sinusoidal endothelium. **Notch**-2 expression displayed a wider distribution and was detectable in hepatocytes, medium sized bile ducts and the sinusoidal endothelium. **Notch**-3 expression was found again in hepatocytes, with weaker expression detectable in portal veins, hepatic arteries and the sinusoids. Taken together these results provide insight into possible cell-cell interactions and signaling events occurring between the receptor and **ligand** expressing cell types in the adult liver. To explore this further, the activity of modifiers that act downstream of **Notch** activation, is also being investigated.

L8 ANSWER 12 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AB. . . affect specific interactions have been described. One particularly intriguing example is the role of the O-linked carbohydrate modifications on the **Notch** proteins. The **Notch** proteins are signaling receptors that play key roles in a wide variety of developmental cascades. They become activated upon binding to **ligands** (e.g., Delta, Serrate/**Jagged**) on adjacent cells. Signaling from the **ligands** can be modulated by the Fringe proteins, potentiating the signaling from some **ligands** (e.g. Delta) while inhibiting signaling from others (e.g. Serrate). Interestingly, the Fringe proteins share regions of homology with several bacterial glycosyltransferases, suggesting that they may function by altering the carbohydrate structures on **Notch**. We have recently demonstrated that **Notch** is modified with two unusual forms of O-linked glycosylation, O-fucose and O-glucose, on its tandem epidermal growth factor-like repeats, providing. . . our and other laboratories has shown that the Fringe proteins are glycosyltransferases, acting by elongation of the O-fucose moieties on **Notch**. Mutation of a conserved acidic region in Drosophila Fringe inactivates its enzymatic activity in vitro and its biological activity in vivo, suggesting that the glycosyltransferase activity is essential for Fringe to mediate its biological effects on **Notch**. These and other results strongly argue that Fringe modulates **Notch** function through alterations in the O-fucose modifications on the **Notch** protein, providing a prime example of how alterations in a specific carbohydrate structure on a cell surface receptor can modulate. . .

L8 ANSWER 13 OF 76 MEDLINE DUPLICATE 8
AB OBJECTIVE: Serrate/**Jagged** and Delta are cell surface **ligands** for **Notch** receptors that may influence hematopoietic cell fate decisions and are known to be expressed in bone marrow stromal cells. In a series of screenings of cDNAs constructed by a

cDNA library subtraction technique, we identified Jagged1, one of the **Notch ligands**, as a gene up-regulated by macrophage colony-stimulating factor (M-CSF) in bone marrow macrophages. Therefore, we compared stromal cells and macrophages for expression of **Notch ligands** including Jagged1 and analyzed the regulation of their expression by cytokines. MATERIALS AND METHODS: Murine bone marrow macrophages were prepared. . . M-CSF. Primary bone marrow fibroblastic stromal cells were prepared by a culture system that we recently developed. The expression of **Notch ligands** was analyzed by either Northern blot analysis or reverse transcriptase polymerase chain reaction. RESULTS: The bone marrow macrophages expressed Jagged1. . .

L8 ANSWER 14 OF 76 MEDLINE DUPLICATE 9
AB . . . syndecan-1 processing and to cell invasion, chemokine receptors CCR1 and CCR2, the Wnt pathway actor Frizzled-related protein (FRZB), and the **Notch** receptor **ligand Jagged** 2. These data, obtained with the Atlas cDNA array, were confirmed by reverse transcriptase-polymerase chain reaction or protein analysis or. . .

L8 ANSWER 15 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
IT . . .
of Organisms
biliary epithelial cell: digestive system
IT Diseases
primary biliary cirrhosis: digestive system disease
IT Chemicals & Biochemicals
CCL28; **Jagged**-1: expression; **Notch ligand**
: expression; TFF3: expression; cell adhesion molecules
IT Alternate Indexing
Liver Cirrhosis, Biliary (MeSH)

L8 ANSWER 16 OF 76 MEDLINE DUPLICATE 10
AB Cell fate of hematopoietic progenitors is regulated by interaction between **Notch** proteins on progenitors and **Notch ligands** such as Jagged1 on stromal cells. Since acute myeloid leukemia (AML) originates from dysregulated hematopoietic progenitors, some abnormalities in the **Notch**-**Jagged** system may exist in AML cells. As the first step to clarify this, we examined the expression of Notch1 and. . . We showed that Notch1 and Jagged1 proteins are widely expressed in AML cells. We hypothesize that some abnormalities in the **Notch**-**Jagged** system which cause the excessive self-renewal and the block of differentiation, may be involved in the abnormal proliferation of AML. . .

L8 ANSWER 17 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
IT . . .
Development
IT Parts, Structures, & Systems of Organisms
epidermis: integumentary system, maturation; keratinocytes: differentiation, integumentary system
IT Chemicals & Biochemicals
Jagged-1; **Notch**: activation; **Notch** 1 receptor; **Notch** 2 receptor; **Notch** 3 receptor; **Notch ligand**

L8 ANSWER 18 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI **Notch** 1 and its **ligand Jagged** 2 expression in the rat testis.

L8 ANSWER 19 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI **Notch ligands** Delta-1 and **Jagged**-1 trigger different signaling pathways in human lymphoid differentiation.
AB **Notch** proteins influence cell-fate decision phenomena in lymphopoiesis. We have previously shown that two **Notch ligands** Delta-1 and **Jagged**-1 can mediate differential effects of **Notch** signaling in human lymphopoiesis. In an attempt to unravel the biological reasons that might underlie these differences we have studied the expression of known target genes of **Notch** signaling in CD34+ cells co-cultured with transduced stromas expressing Delta-1 or **Jagged**-1, using real-time RT-PCR. We observed a marked upregulation of HES-1 expression in progenitor cells cultured in the presence of Delta-1,. . . was decreased 0.5 fold and Deltex virtually unchanged. A different pattern was observed in cells cultured in the presence of **Jagged**-1, where E47 expression was upregulated and HES-1 only modestly increased. A decrease in the expression of Deltex was detected in the latter experimental condition. Though preliminary, our data suggest that Delta-1 and **Jagged**-1 might trigger distinct **Notch** signaling pathways in developing hematopoietic cells.
IT . . .
Biology)
IT Parts, Structures, & Systems of Organisms
lymphoid cells: blood and lymphatics, immune system
IT Chemicals & Biochemicals
Delta-1: **Notch ligands**; **Jagged**-1: **Notch ligands**

L8 ANSWER 20 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Differential effects of **Notch ligands** Delta-1 and **Jagged**-1 in human lymphoid differentiation.
AB **Notch** signaling is known to differentially affect the development of lymphoid B and T-cell lineages, but it remains unclear whether such effects are specifically dependent on distinct **Notch ligands**. Using a cell co-culture assay we observed that the **Notch ligand** Delta-1 completely inhibits the differentiation of human hematopoietic progenitors into the B-cell lineage while promoting the emergence of cells with a phenotype of T/NK precursors. In contrast, **Jagged**-1 did not disturb either B or T/NK development. Furthermore, cells cultured in the presence of either Delta-1 or **Jagged**-1 can acquire a phenotype of NK-cells, and Delta-1, but not **Jagged**-1, permits the emergence of a de novo cell population coexpressing CD4 and CD8. Our results thus indicate that distinct **Notch ligands** can mediate differential effects of **Notch** signaling and provide a useful system to further address cell-fate decision processes in lymphopoiesis.
IT . . .
Biology)
IT Parts, Structures, & Systems of Organisms
lymphoid cells: blood and lymphatics, immune system
IT Chemicals & Biochemicals
Delta-1: **Notch ligands**; **Jagged**-1: **Notch ligands**

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=> dis his

     (FILE 'HOME' ENTERED AT 11:18:57 ON 24 FEB 2002)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 11:19:07 ON 24 FEB 2002
L1          240 S JAGGED (P) NOTCH
L2            0 S (ADMINIST? (10N) JAGGED) (P) NOTCH
L3            0 S (ADMINIST? (10N) JAGGED)
L4           12 S (ADMINIST? (P) JAGGED)
L5            6 DUP REM L4 (6 DUPLICATES REMOVED)
L6          180 S L1 (P) LIGAND
L7            0 S L6 (P) (PHARMACEUT? OR THERAP?)
L8           76 DUP REM L6 (104 DUPLICATES REMOVED)

=> dis l8 1-17 ibib abs

L8   ANSWER 1 OF 76     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:   2001466773     MEDLINE
DOCUMENT NUMBER:    21402959   PubMed ID: 11427524
TITLE:              Soluble Jagged 1 represses the function of its
                    transmembrane form to induce the formation of the
                    Src-dependent chord-like phenotype.
AUTHOR:             Small D; Kovalenko D; Kacer D; Liaw L; Landriscina M; Di
                    Serio C; Prudovsky I; Maciag T
CORPORATE SOURCE:   Center for Molecular Medicine, Maine Medical Center
                    Research Institute, Scarborough, Maine 04074, USA.
CONTRACT NUMBER:    HL3567 (NHLBI)
                    NRSA-CA92255 (NINR)
                    RR1555 (NCRR)
SOURCE:             JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Aug 24) 276 (34)
                    32022-30.
                    Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:       United States
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200109
ENTRY DATE:         Entered STN: 20010821
                    Last Updated on STN: 20010924
                    Entered Medline: 20010920
AB   We have previously demonstrated that the expression of the soluble
     extracellular domain of the transmembrane ligand for
     Notch receptors, Jagged 1 (sJ1), in NIH 3T3 cells
     results in the formation of a matrix-dependent chord-like phenotype, the
     loss of contact inhibition of growth, and an inhibition of pro-alpha 1(I)
     collagen expression. In an effort to define the mechanism by which sJ1
     induces this phenotype, we report that sJ1 transfectants display
     biochemical and cytoskeletal alterations consistent with the activation of
     Src. Indeed, cotransfection of sJ1 transfectants with a dominant-negative
     mutant of Src resulted in the loss of matrix-dependent chord formation and
     correlated with the restoration of type I collagen expression and contact
     inhibition of growth. We also report that the sJ1-mediated induction of
     Src activity and related phenotypes, including chord formation, may result
     from the inhibition of endogenous Jagged 1-mediated
     Notch signaling since it was not possible to detect an
     sJ1-dependent induction of CSL-dependent transcription in these cells.
     Interestingly, NIH 3T3 cells transfected with dominant-negative (but not
     constitutively active) mutants of either Notch 1 or
     Notch 2 displayed a similar Src-related phenotype as the sJ1
     transfectants. These data suggest that the ability of sJ1 to mediate chord
     formation is Src-dependent and requires the repression of endogenous
     Jagged 1-mediated Notch signaling, which is tolerant to
     the destabilization of the actin cytoskeleton, a mediator of cell
     migration.

L8   ANSWER 2 OF 76     MEDLINE                          DUPLICATE 2
ACCESSION NUMBER:   2001255726     MEDLINE
DOCUMENT NUMBER:    21244657   PubMed ID: 11344305
TITLE:              Vascular patterning defects associated with expression of
                    activated Notch4 in embryonic endothelium.
COMMENT:            Comment in: Proc Natl Acad Sci U S A. 2001 May
                    8;98(10):5377-8
AUTHOR:             Uyttendaele H; Ho J; Rossant J; Kitajewski J
CORPORATE SOURCE:   Department of Pathology and Obstetrics/Gynecology, Columbia
                    University, 630 West 168th Street, New York, NY 10032, USA.
CONTRACT NUMBER:    RO1 HL62454 (NHLBI)
SOURCE:             PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE
                    UNITED STATES OF AMERICA, (2001 May 8) 98 (10) 5643-8.
                    Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY:       United States
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200106
ENTRY DATE:         Entered STN: 20010618
                    Last Updated on STN: 20010618
                    Entered Medline: 20010614
AB   Notch proteins function as receptors for membrane-bound
     ligands (Jagged and Delta-like) to regulate cell-fate
     determination. We have investigated the role of Notch signaling
     in embryonic endothelium of the mouse by expressing an activated form of
     the Notch4 protein in vasculature under the regulation of the Flk1 (VEGFR)
     locus. Expression of activated Notch4 results in a growth and
     developmental delay and embryonic lethality at about 10 days postcoitum.
     The extent of the developing vasculature in mutant embryos was restricted,
     fewer small vessels were seen, and vascular networks were disorganized.
     The brain periphery of mutant embryos contained large dilated vessels with
     evidence of compromised vessel-wall integrity and large areas of necrosis;
     yolk-sac vasculature was abnormal. Expression of an activated form of
     Notch4 in embryonic vasculature leads to abnormal vessel structure and
     patterning, implicating the Notch pathway in phases of vascular
     development associated with vessel patterning and remodeling.

L8   ANSWER 3 OF 76  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER:   2001:221312  BIOSIS
DOCUMENT NUMBER:    PREV200100221312
TITLE:              The Notch ligand Jagged1 is required for inner ear sensory
                    development.
AUTHOR(S):          Kiernan, Amy E.; Ahituv, Nadav; Fuchs, Helmut; Balling,
                    Rudi; Avraham, Karen B.; Steel, Karen P. (1); de Angelis,
                    Martin Hrabe
CORPORATE SOURCE:   (1) Medical Research Council Institute of Hearing Research,
```

University Park, Nottingham, NG7 2RD: karen@ihr.mrc.ac.uk
UK
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (March 27, 2001) Vol. 98, No. 7, pp. 3873-3878. print.
ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Within the mammalian inner ear there are six separate sensory regions that subserve the functions of hearing and balance, although how these sensory regions become specified remains unknown. Each sensory region is populated by two cell types, the mechanosensory hair cell and the supporting cell, which are arranged in a mosaic in which each hair cell is surrounded by supporting cells. The proposed mechanism for creating the sensory mosaic is lateral inhibition mediated by the Notch signaling pathway. However, one of the Notch ligands, Jagged1 (Jag1), does not show an expression pattern wholly consistent with a role in lateral inhibition, as it marks the sensory patches from very early in their development-presumably long before cells make their final fate decisions. It has been proposed that Jag1 has a role in specifying sensory versus nonsensory epithelium within the ear (Adam, J., Myat, A., Roux, I. L., Eddison, M., Henrique, D., Ish-Horowicz, D. & Lewis, J. (1998) Development (Cambridge, U.K.) 125, 4645-4654). Here we provide experimental evidence that Notch signaling may be involved in specifying sensory regions by showing that a dominant mouse mutant headturner (Htu) contains a missense mutation in the Jag1 gene and displays missing posterior and sometimes anterior ampullae, structures that house the sensory cristae. Htu/+ mutants also demonstrate a significant reduction in the numbers of outer hair cells in the organ of Corti. Because lateral inhibition mediated by Notch predicts that disruptions in this pathway would lead to an increase in hair cells, we believe these data indicate an earlier role for Notch within the inner ear.

L8 ANSWER 4 OF 76 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001696681 MEDLINE
DOCUMENT NUMBER: 21610601 PubMed ID: 11745352
TITLE: Notch ligand-bearing thymic epithelial cells initiate and sustain Notch signaling in thymocytes independently of T cell receptor signaling.
AUTHOR: Anderson G; Pongracz J; Parnell S; Jenkinson E J
CORPORATE SOURCE: Department of Anatomy, MRC Centre for Immune Regulation, Division of Immunity and Infection, Medical School, University of Birmingham, Edgbaston, Birmingham, GB.. g.anderson@bham.ac.uk
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (2001 Nov) 31 (11) 3349-54. Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: Germany: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011218
Last Updated on STN: 20020125
Entered Medline: 20020103
AB Thymic epithelial cells are specialized to play essential roles at multiple stages of T cell development in the thymus, yet the molecular basis of this specialization is largely unknown. Recently, the **Notch** family of transmembrane proteins has been implicated in thymocyte development. Such proteins interact with cell surface proteins of the Delta-like and **Jagged** families. It is known that **Notch ligands** are expressed intrathymically, and that **Notch** signaling is regulated by **Notch ligands** expressed on either the same or third-party cells. However, functional analysis of **Notch ligand** expression, and elucidation of the mechanism of **Notch ligand** signaling in thymocyte development, are unclear. Here, we find that **Notch ligand** expression in the thymus is compartmentalized, with MHC class II(+) thymic epithelium, but not thymocytes nor dendritic cells, expressing **Jagged**-1, **Jagged**-2 and Delta-like-1. We also provide evidence that contact with **Notch ligands** on thymic epithelium is necessary to activate and sustain **Notch** signaling in thymocytes, and that this can occur independently of positive selection induction. Our data suggest that **Notch ligand** expression by thymic epithelium may partly explain the specialization of these cells in supporting thymocyte development, by regulating **Notch** activation via an inductive signaling mechanism independently of signaling leading to positive selection.

L8 ANSWER 5 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:562550 BIOSIS
DOCUMENT NUMBER: PREV200100562550
TITLE: Neuronal induction of Notch signaling in glia induces erbB receptor expression and radial glia differentiation.
AUTHOR(S): Corfas, G. (1); Weinmaster, G.; Temple, S.; Peyrin, J. M. (1)
CORPORATE SOURCE: (1) Div Neurosci, Children's Hosp, Boston, MA USA
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 1817. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Radial glia are critical for brain development. We previously showed that Bergmann glia express erbB receptors, that activation of these receptors is essential for radial glia differentiation, and that erbB receptor expression by radial glia is developmentally regulated. To understand the mechanisms of radial glia differentiation we studied the regulation of erbB receptor expression in these cells. We now show that **Notch** and its **ligands** are critical in these events. In the developing cerebellum Notch1 is expressed by Bergmann glia and granule cells express **Notch ligands**. Using neuron-glia co-cultures we show that granule cells induce **Notch** signaling in cerebellar astrocytes and also induce the expression of erbB2 receptors in glia as they do with BLBP, a radial glia protein. **Notch** signaling is necessary and sufficient for these effects, since contact with **Jagged**-expressing fibroblast or expression of an activated form of **Notch** lead to the same changes in glia as neuronal contact, and expression of a dominant-negative **Notch** in glia abolishes the effect of neuronal contact. In contrast, erbB receptor activation does not

induce erbB2 or BLBP expression. Finally, blocking **Notch** signaling also blocks the ability of neurons to induce radial glia formation to the same extent as a DN-erbB receptor. Our results suggest that **Notch** signaling is an early step in the program of neuronal-induced radial glia differentiation, and that this is mediated by inducing erbB receptor expression, which is necessary for the final differentiation of the glia cell into a functional partner for migrating neurons.

L8 ANSWER 6 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:259789 BIOSIS
DOCUMENT NUMBER: PREV200100259789
TITLE: Notch receptor expression in human fetal and paediatric liver.
AUTHOR(S): Flynn, Diana M. (1); Nijjar, Sarbjit (1); Hubscher, Stefan G. (1); de Ville de Goyet, Jean (1); Kelly, Deirdre A. (1); Kilby, Mark D. (1); Strain, Alastair J. (1); Crosby, Heather A. (1)
CORPORATE SOURCE: (1) Queen Elizabeth Hospital, Birmingham University, Birmingham, B15 2TH UK
SOURCE: FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1084. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Notch** signaling is important in normal development and cell specification in many organisms. Jagged1, a **notch** receptor **ligand**, is present in developing liver and implicated in the abnormal development of the biliary tree in Alagille syndrome. In this study Notch1-4 receptor expression was examined in fetal, normal and diseased paediatric liver. RT-PCR for Jagged1 and Notch1-4 was performed in human paediatric normal (n=5) and diseased liver (n=10). Immunostaining of frozen sections of fetal (n=4; 10-16 weeks), normal (n=7; 4-12 years), extrahepatic biliary atresia (EHBA; n=7; 9 months-4 years), and alantitrypsin deficiency (AIAT; n=4, 1-5 years) liver was performed using antibodies to Notch1-4, Jagged1 and cytokeratin 19 (CK19). Jagged1 and Notch1-4 mRNA expression was detectable in all samples by RT-PCR. Immunostaining fetal liver showed Jagged1 expression only on ductal plate (colocalised with CK19) and on vascular endothelium, and Notch3 on adjacent portal tract mesenchyme. In normal liver, Notch1-4 stained endothelial cells, additionally Notch2 and 3 also stained occasional biliary epithelial cells (BEC) and **Jagged** 1 colocalised with CK19 on BEC. In diseased tissue, Notch2 additionally stained stromal cells in portal tracts and cirrhotic fibrous septa, Notch3 was also strongly positive on stromal cells and occasional ductular cells, and Jagged1 colocalised with CK19 on ductular cells. Notch3 is expressed in developing liver in close proximity to ductal plate cells. Its expression is limited in normal paediatric liver but is increased in areas of marginal ductular reaction in disease associated with bile duct loss. Its close proximity to Jagged1 expressing cells in these areas suggests that Notch3 may be required for normal development of bile ducts and may be reactivated in paediatric liver diseases associated with bile duct loss where ductular reaction occurs.

L8 ANSWER 7 OF 76 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001490110 MEDLINE
DOCUMENT NUMBER: 21423517 PubMed ID: 11532344
TITLE: Notch receptors and hematopoiesis.
AUTHOR: Kojika S; Griffin J D
CORPORATE SOURCE: Department of Adult Oncology, Dana Farber Cancer Institute, Boston, MA 02115, USA.
SOURCE: EXPERIMENTAL HEMATOLOGY, (2001 Sep) 29 (9) 1041-52. Ref: 151
Journal code: EPR; 0402313. ISSN: 0301-472X.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010905
Last Updated on STN: 20011001
Entered Medline: 20010927
AB **Notch** receptors are involved in a variety of cell-fate decisions that affect the development and function of many organs, including hematopoiesis and the immune system. There are four mammalian **Notch** receptors that have only partially overlapping functions despite sharing similar structures and **ligands**. The **ligands** for **Notch** are transmembrane proteins expressed on adjacent cells, including **Jagged** and Delta, and it is quite possible that signaling is bidirectional. A large **Notch** precursor protein is proteolytically cleaved to form the mature cell-surface receptor. **Ligand** binding induces additional proteolytic events followed by translocation of the intracellular domain to the nucleus. There, **Notch** interacts with transcription factors such as RBPJ kappa, activating transcription of basic helix-loop-helix genes such as HES1. These in turn regulate expression of tissue-specific transcription factors that influence lineage commitment and other events. In this review, the details of **Notch** signaling will be discussed, with a focus on what is known about the role of **Notch** in hematopoiesis.

L8 ANSWER 8 OF 76 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001648460 IN-PROCESS
DOCUMENT NUMBER: 21557592 PubMed ID: 11700865
TITLE: Requirement of **Notch** 1 and its **ligand** **jagged** 2 expressions for spermatogenesis in rat and human testes.
AUTHOR: Hayashi T; Kageyama Y; Ishizaka K; Xia G; Kihara K; Oshima H
CORPORATE SOURCE: Department of Urology and Reproductive Medicine, Graduate School, Tokyo Medical and Dental University, Japan.
SOURCE: JOURNAL OF ANDROLOGY, (2001 Nov-Dec) 22 (6) 999-1011.
Journal code: 8106453. ISSN: 0196-3635.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 20011112
Last Updated on STN: 20020123

AB It has already been demonstrated that the Notch signaling system is essential for gametogenesis in the adult germ line of Caenorhabditis elegans. However, the role of the Notch signaling system in mammalian spermatogenesis has not been well investigated. Recently, it has been revealed that this signaling system is expressed in the mammalian testis by showing coexpression of Jagged 2 and its receptor, Notch 1, is consistent with Notch 1 being a cognate receptor for Jagged 2 in the mammalian testis. Therefore, we investigated expressions of messenger RNAs of Notch 1 and Jagged 2 in the testicular tissues of developing Sprague-Dawley rats by reverse transcription-polymerase chain reaction and Northern blot analysis, expressions of their proteins in the testicular tissues of developing rats, fertile human controls and infertile human patients with maturation arrest by immunohistochemistry, and effects of antibodies to this system by culturing rat testicular tissues with these antibodies. Transcripts of Notch 1 and Jagged 2 in the rat testis were positive throughout the examined period; these intensities became higher at day 13 after birth, coincidence with the formation of spermatocytes, and peaked at day 19 after birth. Expressions of Notch 1 and Jagged 2 were recognized at first in the perinuclear regions of spermatocytes in the rat testis as a round structure at day 19 after birth and thereafter in further differentiated germ cells as meiosis proceeded. In the adult rat testis, positive staining was present as a round structure in spermatocytes, as a typical horseshoe-shaped structure in round spermatids, and as a covering structure spreading around the nucleus of elongated spermatids, but not in spermatozoa. Notch 1 was recognized in the vacuole of the Golgi complex of primary spermatocytes and the acrosome of elongated spermatids with electron microscopy. When rat testicular tissues were cultured with anti-Notch 1 or anti-Jagged 2 antibody, round and elongated spermatids decreased after 5 and 7 days of culture, respectively, and disappeared at around 9 and 12 days of culture, respectively, with shrinkage of the diameter of seminiferous tubules. Spermatocytes, however, increased after 11 days of culture. Expressions of both proteins have been detected in the testicular tissues of human fertile controls as in the rat testicular tissues. However, Notch 1 expression has not been detected in testicular tissues of 11 patients with maturation arrest, whereas Jagged 2 expression has been recognized in all of them. In conclusion, the results presented in this study offer the possibility that Notch 1/Jagged 2 signaling system plays an important role for male germ cells to differentiate or at least to survive in the rat testis and fails to express in the testis of spermatogenic maturation arrest patients.

L8 ANSWER 9 OF 76 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2001534256 MEDLINE
DOCUMENT NUMBER: 21464863 PubMed ID: 11581320
TITLE: Differential effects of **Notch ligands** Delta-1 and **Jagged**-1 in human lymphoid differentiation.
COMMENT: Comment in: J Exp Med. 2001 Oct 1;194(7):F43-6
AUTHOR: Jaleco A C; Neves H; Hooijberg E; Gameiro P; Clode N; Haury M; Henrique D; Parreira L
CORPORATE SOURCE: Instituto de Histologia e Embriologia, Faculdade de Medicina de Lisboa, 1649-028 Lisboa, Portugal.
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (2001 Oct 1) 194 (7) 991-1002.
Journal code: I2V; 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200111
ENTRY DATE: Entered STN: 20011003
Last Updated on STN: 20011105
Entered Medline: 20011101

AB **Notch** signaling is known to differentially affect the development of lymphoid B and T cell lineages, but it remains unclear whether such effects are specifically dependent on distinct **Notch ligands**. Using a cell coculture assay we observed that the **Notch ligand** Delta-1 completely inhibits the differentiation of human hematopoietic progenitors into the B cell lineage while promoting the emergence of cells with a phenotype of T cell/natural killer (NK) precursors. In contrast, **Jagged**-1 did not disturb either B or T cell/NK development. Furthermore, cells cultured in the presence of either Delta-1 or **Jagged**-1 can acquire a phenotype of NK cells, and Delta-1, but not **Jagged**-1, permits the emergence of a de novo cell population coexpressing CD4 and CD8. Our results thus indicate that distinct **Notch ligands** can mediate differential effects of **Notch** signaling and provide a useful system to further address cell-fate decision processes in lymphopoiesis.

L8 ANSWER 10 OF 76 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 2001648453 IN-PROCESS
DOCUMENT NUMBER: 21557585 PubMed ID: 11700858
TITLE: Expression of Notch pathway components in spermatogonia and Sertoli cells of neonatal mice.
AUTHOR: Dirami G; Ravindranath N; Achi M V; Dym M
CORPORATE SOURCE: Department of Cell Biology, Georgetown University Medical Center, Washington, DC 20007, USA.
CONTRACT NUMBER: HD-33728 (NICHD)
SOURCE: JOURNAL OF ANDROLOGY, (2001 Nov-Dec) 22 (6) 944-52.
Journal code: 8106453. ISSN: 0196-3635.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20011112
Last Updated on STN: 20020123

AB Members of the **Notch** gene family have been shown to play an important role in the control of cell fate in many developmental systems. We hypothesized that the fate of the male germ line stem cells may also be mediated through the **Notch** signaling pathway. We therefore sought to determine whether the components of the **Notch** pathway are expressed in the mouse testis. Western blot analysis revealed the expression of three **Notch** receptors (**Notch** 1, **Notch** 2, and **Notch** 3), **Notch ligands** (**Jagged** 1, **Jagged** 2, and Delta 1), and presenilin 1 (PS1) in neonatal mouse testis. We then examined their cellular localization by immunohistochemical analysis of cocultures of spermatogonia and Sertoli cells. The 3 **Notch** receptors were found to be expressed in spermatogonia. Sertoli cells expressed only

Notch 2 receptor. Among the **Notch ligands**, Delta 1 and **Jagged** 1 were localized exclusively in spermatogonia and Sertoli cells, respectively. PS1 was apparent in both spermatogonia and Sertoli cells. The presence of **Notch** receptors and **Notch ligands** in spermatogonia and Sertoli cells indicates that these cells are capable of responding to and eliciting **Notch** signaling during the process of spermatogenesis. Key words: Cell fate, delta, **jagged**, presenilin, spermatogenesis.

L8 ANSWER 11 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:248934 BIOSIS
DOCUMENT NUMBER: PREV200100248934
TITLE: Expression of Notch receptors and their ligands in adult human liver.
AUTHOR(S): Nijjar, Sarbjit S. (1); Crosby, Heather A. (1); Wallace, Lorraine (1); Strain, Alastair J. (1)
CORPORATE SOURCE: (1) Liver Research Laboratories, Queen Elizabeth Hospital, University of Birmingham, Edgbaston, Birmingham, West Midlands, B15 2TH UK
SOURCE: FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A943. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Notch** signaling is an evolutionarily conserved mechanism, used to regulate cell fate decisions. Four **Notch** receptors have been identified in man (**Notch**-1 to -4), together with two **Notch ligand** families, Delta (Delta-1, -3 and -4) and Serrate/**Jagged** (**Jagged**-1 and -2). Using total RNA isolated from whole tissue, semi-quantitative RT-PCR was used to determine which **Notch** signaling components were expressed in the adult liver and whether their expression was perturbed in disease. Although no significant differences in the levels of expression for the **Notch** receptors was seen, the expression of **Jagged**-1 was found to be elevated in primary biliary cirrhosis and primary sclerosing cholangitis liver. **Jagged**-2 and Delta-1 gene expression was not detectable in normal or diseased liver. To localise **Notch** receptor and **ligand** expression, purified cell types were isolated from normal and diseased liver. Semi-quantitative RT-PCR using RNA isolated from cells, together with immunostaining of liver sections revealed that **Jagged**-1 expression was present in hepatocytes, bile ducts and the vasculature. The distribution of **Notch**-1 and -4 was similar, with both receptors detectable at low levels in hepatocytes and the sinusoidal endothelium. **Notch**-2 expression displayed a wider distribution and was detectable in hepatocytes, medium sized bile ducts and the sinusoidal endothelium. **Notch**-3 expression was found again in hepatocytes, with weaker expression detectable in portal veins, hepatic arteries and the sinusoids. Taken together these results provide insight into possible cell-cell interactions and signaling events occurring between the receptor and **ligand** expressing cell types in the adult liver. To explore this further, the activity of modifiers that act downstream of **Notch** activation, is also being investigated.

L8 ANSWER 12 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:263652 BIOSIS
DOCUMENT NUMBER: PREV200100263652
TITLE: Fringe modulates the notch signaling pathway by altering O-linked carbohydrate structures on notch.
AUTHOR(S): Haltiwanger, Robert S. (1)
CORPORATE SOURCE: (1) Biochemistry and Cell Biology, State University of New York at Stony Brook, Stony Brook, NY, 11794-5215 USA
SOURCE: FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A864. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Carbohydrate modifications on proteins have long been proposed to play a role in the interactions that occur at cell surfaces. Recently several examples of how specific carbohydrate structures affect specific interactions have been described. One particularly intriguing example is the role of the O-linked carbohydrate modifications on the **Notch** proteins. The **Notch** proteins are signaling receptors that play key roles in a wide variety of developmental cascades. They become activated upon binding to **ligands** (e.g., Delta, Serrate/**Jagged**) on adjacent cells. Signaling from the **ligands** can be modulated by the Fringe proteins, potentiating the signaling from some **ligands** (e.g. Delta) while inhibiting signaling from others (e.g. Serrate). Interestingly, the Fringe proteins share regions of homology with several bacterial glycosyltransferases, suggesting that they may function by altering the carbohydrate structures on **Notch**. We have recently demonstrated that **Notch** is modified with two unusual forms of O-linked glycosylation, O-fucose and O-glucose, on its tandem epidermal growth factor-like repeats, providing potential targets for Fringe action. Work in our and other laboratories has shown that the Fringe proteins are glycosyltransferases, acting by elongation of the O-fucose moieties on **Notch**. Mutation of a conserved acidic region in Drosophila Fringe inactivates its enzymatic activity in vitro and its biological activity in vivo, suggesting that the glycosyltransferase activity is essential for Fringe to mediate its biological effects on **Notch**. These and other results strongly argue that Fringe modulates **Notch** function through alterations in the O-fucose modifications on the **Notch** protein, providing a prime example of how alterations in a specific carbohydrate structure on a cell surface receptor can modulate a signaling event.

L8 ANSWER 13 OF 76 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 2001384568 MEDLINE
DOCUMENT NUMBER: 21331561 PubMed ID: 11438207
TITLE: Expression of Jagged1 gene in macrophages and its regulation by hematopoietic growth factors.
AUTHOR: Nomaguchi K; Suzu S; Yamada M; Hayasawa H; Motoyoshi K
CORPORATE SOURCE: Biochemical Research Laboratory, Morinaga Milk Industry Co., Ltd., Kanagawa, Japan.
SOURCE: EXPERIMENTAL HEMATOLOGY, (2001 Jul) 29 (7) 850-5.

Journal code: EPR; 0402313. ISSN: 0301-472X.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20010820
Entered Medline: 20010816

AB OBJECTIVE: Serrate/**Jagged** and Delta are cell surface **ligands** for **Notch** receptors that may influence hematopoietic cell fate decisions and are known to be expressed in bone marrow stromal cells. In a series of screenings of cDNAs constructed by a cDNA library subtraction technique, we identified Jagged1, one of the **Notch ligands**, as a gene up-regulated by macrophage colony-stimulating factor (M-CSF) in bone marrow macrophages. Therefore, we compared stromal cells and macrophages for expression of **Notch ligands** including Jagged1 and analyzed the regulation of their expression by cytokines. MATERIALS AND METHODS: Murine bone marrow macrophages were prepared by culturing femoral bone marrow cells with M-CSF. Primary bone marrow fibroblastic stromal cells were prepared by a culture system that we recently developed. The expression of **Notch ligands** was analyzed by either Northern blot analysis or reverse transcriptase polymerase chain reaction. RESULTS: The bone marrow macrophages expressed Jagged1 but not Jagged2 and Delta1 at a level that was detectable by Northern blot analysis. Expression of the Jagged1 gene was markedly up-regulated by growth factors for the cells, i.e., M-CSF, granulocyte-macrophage colony-stimulating factor, and interleukin-3. Expression of Jagged2 and Delta1 seldom was affected by the stimuli. The primary bone marrow fibroblastic stromal cells, and murine stromal cell lines, such as PA6 and ST2, also expressed Jagged1 transcript, at levels comparable to the steady-state level in macrophages. However, expression of the Jagged1 gene was little affected when these cells were stimulated with fibroblastic growth factor and platelet-derived growth factor. CONCLUSIONS: We demonstrated that bone marrow macrophages as well as stromal cells constitutively produced Jagged1 and that the expression was markedly up-regulated by hematopoietic growth factors, M-CSF, granulocyte-macrophage colony-stimulating factor, and interleukin-3. The results highlight the involvement of macrophages and these growth factors in hematopoietic cell fate decisions via the production of Jagged1.

L8 ANSWER 14 OF 76 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 2001420323 MEDLINE
DOCUMENT NUMBER: 21361178 PubMed ID: 11468178
TITLE: Identifying intercellular signaling genes expressed in malignant plasma cells by using complementary DNA arrays.
AUTHOR: De Vos J; Couderc G; Tarte K; Jourdan M; Requirand G; Delteil M C; Rossi J F; Mechti N; Klein B
CORPORATE SOURCE: INSERM U475, Unit for Cellular Therapy, CHU Montpellier, 99 Rue Puech Villa, 34197 Montpellier Cedex 5, France.
SOURCE: BLOOD, (2001 Aug 1) 98 (3) 771-80.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010917
Last Updated on STN: 20010917
Entered Medline: 20010913

AB In multiple myeloma (MM), the growth of primary plasma cells depends not only on interleukin-6 (IL-6), but also on additional unidentified signals delivered by the bone marrow environment. Using Atlas complementary DNA (cDNA) arrays comprising 268 genes coding for intercellular signaling molecules, this study identified genes that are overexpressed in myeloma cells compared to autologous B-lymphoblastoid cell lines. These genes encode the oncogenic Tyro3 tyrosine kinase receptor, the heparin-binding epidermal growth factor-like growth factor (HB-EGF) that is an epithelial autocrine tumor growth factor, the thrombin receptor (TR) that is linked to HB-EGF and syndecan-1 processing and to cell invasion, chemokine receptors CCR1 and CCR2, the Wnt pathway actor Frizzled-related protein (FRZB), and the **Notch** receptor **ligand Jagged** 2. These data, obtained with the Atlas cDNA array, were confirmed by reverse transcriptase-polymerase chain reaction or protein analysis or both. Furthermore, Tyro3, HB-EGF, TR, and FRZB gene expression was documented in purified primary malignant plasma cells from patients with plasma cell leukemia or MM. HB-EGF and FRZB were poorly expressed in purified polyclonal plasma cells. Finally, HB-EGF was proved to be an essential autocrine growth factor for the XG-1 myeloma cells. This study shows the potency and the biologic relevance of cDNA arrays used to analyze simultaneously a large panel of intercellular signaling genes and, by identifying several genes overexpressed in malignant plasma cells, opens new fields of investigation in MM biology. (Blood. 2001;98:771-780)

L8 ANSWER 15 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:141256 BIOSIS
DOCUMENT NUMBER: PREV200200141256
TITLE: Increased expression of Jagged-1 and TFF3 in primary biliary cirrhosis.
AUTHOR(S): Kimura, Yasuhiko (1); Leung, Patrick S.; Kenny, Tom; Van de Water, Judy; Nishioka, Mikio; Gershwin, M. E.
CORPORATE SOURCE: (1) University of California at Davis School of Medicine, Davis, CA USA
SOURCE: Hepatology, (October, 2001) Vol. 34, No. 4 Pt. 2, pp. 525A. http://hepatology.aasldjournals.org/scripts/om.dll/serve?action=searchDB&searchDBfor=home&id=jhep. print.
Meeting Info.: 52nd Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA November 09-13, 2001
ISSN: 0270-9139.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 16 OF 76 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 2001646693 MEDLINE
DOCUMENT NUMBER: 21556729 PubMed ID: 11699411
TITLE: Expression of Notch1 and Jagged1 proteins in acute myeloid leukemia cells.
AUTHOR: Tohda S; Nara N
CORPORATE SOURCE: Department of Laboratory Medicine, Tokyo Medical and Dental University, Yushima 1-5-45, Bunkyo-ku, Tokyo 113-8519, Japan.. tohda.mlab@tmd.ac.jp
SOURCE: LEUKEMIA AND LYMPHOMA, (2001 Jul) 42 (3) 467-72.

Journal code: 9007422. ISSN: 1042-8194.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011112
Last Updated on STN: 20020125
Entered Medline: 20020116

AB Cell fate of hematopoietic progenitors is regulated by interaction between **Notch** proteins on progenitors and **Notch ligands** such as Jagged1 on stromal cells. Since acute myeloid leukemia (AML) originates from dysregulated hematopoietic progenitors, some abnormalities in the **Notch-Jagged** system may exist in AML cells. As the first step to clarify this, we examined the expression of Notch1 and Jagged1 proteins in eight AML cell lines and 15 fresh AML samples by immunoblotting. In the Notch1 protein, two bands, a 300 kDa band and a 120 kDa band, which appeared to be a full-length protein and a transmembrane fragment, respectively, were recognized in five AML cell lines and six fresh samples. In addition, three of the five cell lines showed a 110 kDa fragment, which appeared to be from an intracellular domain, namely an active form. One cell line showed aberrant sized fragments, which suggested a structural abnormality. Jagged1 protein was recognized in six cell lines and six fresh samples. In four cell lines and four fresh samples, both Notch1 and Jagged1 proteins were observed. In these cells, Notch1 and Jagged1 proteins may interact among themselves. We showed that Notch1 and Jagged1 proteins are widely expressed in AML cells. We hypothesize that some abnormalities in the **Notch-Jagged** system which cause the excessive self-renewal and the block of differentiation, may be involved in the abnormal proliferation of AML cells.

L8 ANSWER 17 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:483482 BIOSIS
DOCUMENT NUMBER: PREV200100483482
TITLE: Activation of notch signaling in keratinocytes (KCs) is necessary and sufficient to create mature human epidermis.
AUTHOR(S): Nickoloff, B. (1); Qin, J. (1); Chaturvedi, V. (1); Denning, M. (1); Bonish, B. (1); Miele, L. (1)
CORPORATE SOURCE: (1) Pathology, Loyola University, Chicago, IL USA
SOURCE: Journal of Investigative Dermatology, (August, 2001) Vol. 117, No. 2, pp. 408. print.
Meeting Info.: 62nd Annual Meeting of the Society for Investigative Dermatology Washington, DC, USA May 09-12, 2001
ISSN: 0022-202X.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

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L8 ANSWER 18 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:381562 BIOSIS
DOCUMENT NUMBER: PREV200100381562
TITLE: **Notch** 1 and its **ligand Jagged** 2 expression in the rat testis.
AUTHOR(S): Hayashi, Tetsuo (1); Kageyama, Yukio (1); Kihara, Kazunori (1)
CORPORATE SOURCE: (1) Tokyo Japan
SOURCE: Journal of Urology, (May, 2001) Vol. 165, No. 5 Supplement, pp. 342. print.
Meeting Info.: Annual Meeting of the American Urological Association, Inc. Anaheim, California, USA June 02-07, 2001
ISSN: 0022-5347.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 19 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:151840 BIOSIS
DOCUMENT NUMBER: PREV200200151840
TITLE: **Notch ligands** Delta-1 and **Jagged**-1 trigger different signaling pathways in human lymphoid differentiation.
AUTHOR(S): Neves, Helia C. (1); Gameiro, Paula; Jaleco, Ana C. (1); Clode, Nuno; Parreira, Leonor (1)
CORPORATE SOURCE: (1) Faculdade de Medicina de Lisboa, Instituto de Histologia e Embriologia, Lisboa Portugal
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 2, pp. 118b-119b. http://www.bloodjournal.org/. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 2 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

AB **Notch** proteins influence cell-fate decision phenomena in lymphopoiesis. We have previously shown that two **Notch ligands** Delta-1 and **Jagged**-1 can mediate differential effects of **Notch** signaling in human lymphopoiesis. In an attempt to unravel the biological reasons that might underlie these differences we have studied the expression of known target genes of **Notch** signaling in CD34+ cells co-cultured with transduced stromas expressing Delta-1 or **Jagged**-1, using real-time RT-PCR. We observed a marked upregulation of HES-1 expression in progenitor cells cultured in the presence of Delta-1, when compared with cells cultured with unmodified stroma. In contrast, E47 was decreased 0.5 fold and Deltex virtually unchanged. A different pattern was observed in cells cultured in the presence of **Jagged**-1, where E47 expression was upregulated and HES-1 only modestly increased. A decrease in the expression of Deltex was detected in the latter experimental condition. Though preliminary, our data suggest that Delta-1 and **Jagged**-1 might trigger distinct **Notch** signaling pathways in developing hematopoietic cells.

L8 ANSWER 20 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:151833 BIOSIS
DOCUMENT NUMBER: PREV200200151833
TITLE: Differential effects of **Notch ligands** Delta-1 and **Jagged**-1 in human lymphoid differentiation.
AUTHOR(S): Jaleco, Ana C. (1); Neves, Helia C. (1); Hooijberg, Erik;

Gameiro, Paula; Clode, Nuno; Haury, Matthias; Henrique, Domingos (1); Parreira, Leonor (1)
CORPORATE SOURCE: (1) Faculdade de Medicina de Lisboa, Instituto de Histologia e Embriologia, Lisboa Portugal
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 2, pp. 117b. http://www.bloodjournal.org/. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 2 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB **Notch** signaling is known to differentially affect the development of lymphoid B and T-cell lineages, but it remains unclear whether such effects are specifically dependent on distinct **Notch ligands**. Using a cell co-culture assay we observed that the **Notch ligand** Delta-1 completely inhibits the differentiation of human hematopoietic progenitors into the B-cell lineage while promoting the emergence of cells with a phenotype of T/NK precursors. In contrast, **Jagged**-1 did not disturb either B or T/NK development. Furthermore, cells cultured in the presence of either Delta-1 or **Jagged**-1 can acquire a phenotype of NK-cells, and Delta-1, but not **Jagged**-1, permits the emergence of a de novo cell population coexpressing CD4 and CD8. Our results thus indicate that distinct **Notch ligands** can mediate differential effects of **Notch** signaling and provide a useful system to further address cell-fate decision processes in lymphopoiesis.

L8 ANSWER 21 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:129745 BIOSIS
DOCUMENT NUMBER: PREV200200129745
TITLE: The soluble **Notch ligand**, **Jagged**-1, inhibits proliferation of CD34+ macrophage progenitors.
AUTHOR(S): Araki, Hiroto (1); Katayama, Naoyuki (1); Masuya, Masahiro (1); Hoshino, Natsuki (1); Miyashita, Hiroyuki (1); Sakano, Seiji; Yamaguchi, Motoko (1); Nishii, Kazuhiro (1); Minami, Nobuyuki; Shiku, Hiroshi (1)
CORPORATE SOURCE: (1) Second Department of Internal Medicine, Mie University School of Medicine, Tsu, Mie Japan
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 74a. http://www.bloodjournal.org/. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The **Notch/Notch ligand** system controls diverse cellular processes and cell fate dicisions in various organisms. The proteolytic cleavage generates transmembrane and soluble forms of **Notch ligands**. Although the function of transmembrane form of **Notch ligands** has been extensively studied, the role of their soluble form in human hematopoiesis is not well understood. As we detected the expression of **Notch** receptors, **Notch**-1 and **Notch**-2, on cord blood CD34+ cells as determined by flowcytometry, the activity of a soluble **Notch ligand**, human **Jagged**-1, was examined under serum-deprived conditions, using soluble human **Jagged**-1-IgG1 chimera protein (hJagged-1). Soluble hJagged-1 alone was not effective for colony formation by human cord blood CD34+ cells. Soluble hJagged-1 inhibited myeloid colony formation but not erythroid-mix or erythroid colony formation, in the presence of stem cell factor (SCF), IL-3, GM-CSF, G-CSF, thrombopoietin, and erythropoietin, in a dose-dependent manner. The inhibitory effects of soluble hJagged-1 on colony formation reached a minimal plateau at the concentration of 0.5 to 1 mg/ml. Cytological analysis revealed that the inhibition of myeloid colony formation by soluble hJagged-1 was mainly due to a decrease in the number of macrophage colony. Among various two-factor combinations, we found that M-CSF plus SCF, M-CSF plus IL-6, M-CSF plus flt3 **ligand**, and GM-CSF plus SCF predominantly supported the growth of CFU-M in our culture system. Using these two-factor combinations, we analyzed the effects of soluble hJagged-1 on colony formation. Soluble hJagged-1 led to an inhibition of macrophage colony formation supported by M-CSF plus SCF and GM-CSF plus SCF. The inhibition of CFU-M formation was not observed when soluble hJagged-1 was added to cultures after day 2 of incubation. The suppression of CFU-M formation was not associated with a decrease in colony size. These data demonstrated that soluble hJagged-1 inhibited the growth of macrophage progenitors by acting at the early stage of macrophage development. Direct action of hJagged-1 on CD34+ cells was confirmed by the expression of Hairy Enhancer of Split-1, HES-1. These results suggest that soluble hJagged-1 may regulate human hematopoiesis in the monocyte-macrophage lineage.

L8 ANSWER 22 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:515598 BIOSIS
DOCUMENT NUMBER: PREV200100515598
TITLE: Coming to grips with Notch.
AUTHOR(S): von Boehmer, Harald (1)
CORPORATE SOURCE: (1) Dana-Farber Cancer Institute, Harvard Medical School, 44 Binney St., Boston, MA, 02115: harald_von_boehmer@dfci.harvard.edu USA
SOURCE: Journal of Experimental Medicine, (October 1, 2001) Vol. 194, No. 7, pp. F43-F46. print.
ISSN: 0022-1007.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 23 OF 76 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:59832 CAPLUS
DOCUMENT NUMBER: 132:118342
TITLE: Notch ligand LDE-1 polypeptide from mouse and human capable of suppressing hematopoietic stem cell differentiation and use for growing hematopoietic stem cells in vitro
INVENTOR(S): Yoneya, Takashi; Miyatani, Seiji; Nishikawa, Mitsuo; Ohsawa, Masatake
PATENT ASSIGNEE(S): Kirin Brewery Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 37 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000023674	A2	20000125	JP 1998-197882	19980713

AB Notch ligand genes, LDE-1 (liver derived EGF gene) and encoded polypeptides capable of suppressing the differentiation of hematopoietic stem cell and stimulate the multiplication of hematopoietic stem cell and hematopoietic precursor cell in coexistence with cell stimulating factors are provided. The amino acid and cDNA sequences of the polypeptide from mouse and human are disclosed. Also described are a method of culturing hematopoietic stem cell and hematopoietic precursor cell in the presence of hematopoietic cell stimulating factors such as stem cell growth factor, interleukin-6, interleukin-1, Flt3/Flk2-ligand, and thrombopoietin (TPO), and the reagents required for the culture.

L8 ANSWER 24 OF 76 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 2000387102 MEDLINE
DOCUMENT NUMBER: 20347870 PubMed ID: 10783395
TITLE: Suppression of erythroid but not megakaryocytic differentiation of human K562 erythroleukemic cells by notch-1.
AUTHOR: Lam L T; Ronchini C; Norton J; Capobianco A J; Bresnick E H
CORPORATE SOURCE: University of Wisconsin Medical School, Department of Pharmacology, Molecular and Cellular Pharmacology Program, Madison, Wisconsin 53706, USA.
CONTRACT NUMBER: DK50107 (NIDDK)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Jun 30) 275 (26) 19676-84.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000818
Last Updated on STN: 20000818
Entered Medline: 20000810

AB The **Notch** signal transduction pathway is a highly conserved regulatory system that controls multiple developmental processes. We have established an erythroleukemia cell model to study how **Notch** regulates cell fate and erythroleukemic cell differentiation. K562 and HEL cells expressed the **Notch**-1 receptor and the **Notch ligand Jagged**-1. The stable expression of the constitutively active intracellular domain of **Notch**-1 (NIC-1) in K562 cells inhibited erythroid without affecting megakaryocytic maturation. Expression of antisense **Notch**-1 induced spontaneous erythroid maturation. Suppression of erythroid maturation by NIC-1 did not result from down-regulation of GATA-1 and TAL-1, transcription factors necessary for erythroid differentiation. Microarray gene expression analysis identified genes activated during erythroid maturation, and NIC-1 disrupted the maturation-dependent changes in the expression of these genes. These results show that NIC-1 alters the pattern of gene expression in K562 cells leading to a block in erythroid maturation and therefore suggest that **Notch** signaling may control the developmental potential of normal and malignant erythroid progenitor cells.

L8 ANSWER 25 OF 76 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 2000474171 MEDLINE
DOCUMENT NUMBER: 20438678 PubMed ID: 10980592
TITLE: Ras pathway signals are required for notch-mediated oncogenesis.
AUTHOR: Fitzgerald K; Harrington A; Leder P
CORPORATE SOURCE: Department of Genetics, Harvard Medical School, Howard Hughes Medical Institute, 200 Longwood Avenue, Boston, Massachusetts, MA 02115, USA.
SOURCE: ONCOGENE, (2000 Aug 31) 19 (37) 4191-8.
Journal code: ONC; 8711562. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001012
Last Updated on STN: 20001012
Entered Medline: 20001005

AB The **Notch** genes of C. elegans, Drosophila melanogaster and vertebrates encode receptors responsible for cell fate decisions during development. These **Notch** receptors and their **ligands**, Delta and **Jagged**, have been implicated in several human diseases. Truncated, constitutively active mutant forms of the **Notch** receptor appear to be involved in human T-cell leukemia, mammary carcinomas in mice, and a tumorous germline phenotype in C. elegans. Since activated **Notch** induces solitary tumors in transgenic mice, it is highly likely that collaborating genetic events are required for tumor formation. We have assessed four signal transduction pathways to determine which might play additional roles in malignant transformation in concert with activated Notch4. Our results suggest that transformation by **Notch** does not, as might have been expected, depend on the Src-like kinases Lck and Fyn, nor upon signals from protein kinase A and C (PKA, PKC). Rather, transformation by **Notch** requires active signals from the Erk/MAP kinase and PI-3 kinase pathways downstream of Ras. Oncogene (2000) 19, 4191 - 4198

L8 ANSWER 26 OF 76 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 2001091920 MEDLINE
DOCUMENT NUMBER: 21029661 PubMed ID: 11187898
TITLE: Notch-1 and Notch-2 exhibit unique patterns of expression in human B-lineage cells.
AUTHOR: Bertrand F E; Eckfeldt C E; Lysholm A S; LeBien T W
CORPORATE SOURCE: University of Minnesota Cancer Center, Minneapolis 55455, USA.
CONTRACT NUMBER: R01 CA31685 (NCI)
R01 CA76055 (NCI)
SOURCE: LEUKEMIA, (2000 Dec) 14 (12) 2095-102.
Journal code: LEU. ISSN: 0887-6924.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322

Last Updated on STN: 20010322
Entered Medline: 20010125

AB The **Notch** genes encode a conserved family of receptors that influence developmental fate in many species. Prior studies have indicated that **Notch**-1 and **Notch**-2 signaling influence the development of hematopoietic stems cells and thymocytes, but little is known regarding **Notch** expression and function in B-lineage cells. We analyzed the expression of **Notch** receptors and **Notch ligands** in human B-lineage cells and bone marrow (BM) stromal cells. **Notch**-1 mRNA and protein is expressed throughout normal B cell development and in leukemic B-lineage cells. In contrast, **Notch**-2 expression is limited to pre-B cells expressing low levels of surface mu. The **Notch ligand** Delta is expressed in BM B-lineage cells. The **Notch ligand Jagged**-1 is not expressed in B-lineage cells, but is expressed in BM stromal cells. These results suggest a model wherein lateral signaling between **Notch** and Delta on B-lineage cells and/or **Notch/Jagged**-1 interactions between B-lineage cells and BM stromal cells may regulate human B cell development.

L8 ANSWER 27 OF 76 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 2000155994 MEDLINE
DOCUMENT NUMBER: 20155994 PubMed ID: 10688816
TITLE: A soluble form of human Delta-like-1 inhibits differentiation of hematopoietic progenitor cells.
AUTHOR: Han W; Ye Q; Moore M A
CORPORATE SOURCE: Laboratory of Developmental Hematopoiesis, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.
CONTRACT NUMBER: 1-F32-HL10152-01 (NHLBI)
CA-08748 (NCI)
SOURCE: BLOOD, (2000 Mar 1) 95 (5) 1616-25.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000407
Last Updated on STN: 20000407
Entered Medline: 20000329

AB Two **Notch ligand** families, Delta and Serrate/ **Jagged**, have been identified in vertebrates. Members of the **Jagged** family have been shown to affect in vitro hematopoiesis. To determine whether members of the Delta family might play a similar role in hematopoiesis, we examined the expression of mouse Delta-like-1 (mDll1). mDll1 protein was detected in whole marrow and in a marrow stromal cell line MS-5. At the RNA level, both mDll1 and Notch1 were seen in marrow precursor, differentiated hematopoietic, marrow stromal, and MS-5 cells. We isolated a cDNA encoding the human homologue of mDll1, designated human Delta-like-1 (hDll1). A soluble form of hDll1, hDll1(NDSL), containing the DSL domain and the N-terminal sequences, was expressed and purified from bacteria as a glutathione S-transferase (GST) fusion protein. We observed that hDll1(NDSL) delayed the acquisition of differentiation markers by murine hematopoietic progenitor cells (Lin-) cultured in vitro with cytokines. In addition, it promoted greater expansion (more than 3 times) of the primitive hematopoietic precursor cell population, measured in high-proliferative potential colony assay and day 12 colony-forming unit spleen (CFU-S) assay, than GST controls. We also observed that the percentage of apoptotic cells decreased and that the number of cells in the S-phase of the cell cycle increased in the cultures of Lin(-) cells with hDll1(NDSL). The effects of hDll1(NDSL) were blocked by antibody against the mouse counterpart of hDll1(NDSL), mDll1(NDSL). These observations demonstrate that hDll1 plays a role in mediating cell fate decisions during hematopoiesis. (Blood. 2000;95:1616-1625)

L8 ANSWER 28 OF 76 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 2001053450 MEDLINE
DOCUMENT NUMBER: 20521704 PubMed ID: 11067884
TITLE: The **notch ligand jagged**-1 represents a novel growth factor of human hematopoietic stem cells.
AUTHOR: Karanu F N; Murdoch B; Gallacher L; Wu D M; Koremoto M; Sakano S; Bhatia M
CORPORATE SOURCE: John P. Robarts Research Institute, Developmental Stem Cell Biology, and the Department of Microbiology and Immunology, The University of Western Ontario, London, Ontario, Canada.
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (2000 Nov 6) 192 (9) 1365-72.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001211

AB The **Notch ligand**, **Jagged**-1, plays an essential role in tissue formation during embryonic development of primitive organisms. However, little is known regarding the role of **Jagged**-1 in the regulation of tissue-specific stem cells or its function in humans. Here, we show that uncommitted human hematopoietic cells and cells that comprise the putative blood stem cell microenvironment express **Jagged**-1 and the **Notch** receptors. Addition of a soluble form of human **Jagged**-1 to cultures of purified primitive human blood cells had modest effects in augmenting cytokine-induced proliferation of progenitors. However, intravenous transplantation of cultured cells into immunodeficient mice revealed that human (h)**Jagged**-1 induces the survival and expansion of human stem cells capable of pluripotent repopulating capacity. Our findings demonstrate that hJagged-1 represents a novel growth factor of human stem cells, thereby providing an opportunity for the clinical utility of **Notch ligands** in the expansion of primitive cells capable of hematopoietic reconstitution.

L8 ANSWER 29 OF 76 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 2000145524 MEDLINE
DOCUMENT NUMBER: 20145524 PubMed ID: 10679295
TITLE: A non-transmembrane form of Jagged-1 regulates the formation of matrix-dependent chord-like structures.
AUTHOR: Wong M K; Prudovsky I; Vary C; Booth C; Liaw L; Mousa S; Small D; Maciag T
CORPORATE SOURCE: Division of Hematology-Oncology, University of Pittsburgh

Cancer Institute, Pittsburgh, Pennsylvania 15213, USA.
CONTRACT NUMBER: AG07450 (NIA)
HL32348 (NHLBI)
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2000 Feb 24) 268 (3) 853-9.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000322

AB **Jagged-Notch** interactions regulate a transmembrane **ligand**-receptor signaling pathway involved in the regulation of cell fate determination as well as myoblast and endothelial cell differentiation. To further examine the role of the transmembrane **ligand**, **Jagged**-1, in the regulation of cell differentiation, we stably transfected NIH 3T3 cells with a truncated form of **Jagged**(J)-1, which results in the secretion of a soluble(s) form of the protein. Comparison of gene expression by serial analysis demonstrated that among the 227 transcripts differentially regulated in the sJ-1 transfectants, the expression of the pro-alpha-2(I) collagen transcript and pro-alpha-1(I) collagen translation product was predominantly repressed in sJ-1 transfectants. When plated on extracellular matrices, sJ-1 transfectants formed prominent chord-like structures on type I collagen but not on fibrin, fibronectin, or vitronectin. While the sJ-1 transfectants exhibited growth kinetics similar to control cells and were unable to grow in soft agar, the cells were less sensitive to contact inhibition of growth in vitro and sJ-1 allografts formed tissue masses in nude mice after a prolonged latency period and exhibited an abundance of host-derived microvascular endothelial cells. These data suggest that J-1 may be able to modulate, in a matrix-dependent manner, the organization of cell to cell interactions including its ability to promote the development of chord-like structures. Copyright 2000 Academic Press.

L8 ANSWER 30 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:228430 BIOSIS
DOCUMENT NUMBER: PREV200000228430
TITLE: Discordant expression of **Notch**-1 and -2 compared to **Notch ligands** (**Jagged**, Delta) in psoriatic epidermis.
AUTHOR(S): Miele, L. (1); Bacon, P. E. (1); Chaturvedi, V. (1); Qin, J.-L. (1); Nickoloff, B. J. (1)
CORPORATE SOURCE: (1) Department of Pathology, Cardinal Bernardin Cancer Center, Loyola University, Chicago, IL USA
SOURCE: Journal of Investigative Dermatology, (April, 2000) Vol. 114, No. 4, pp. 758.
Meeting Info.: 61st Annual Meeting of the Society for Investigative Dermatology. Chicago, Illinois, USA May 10-14, 2000
ISSN: 0022-202X.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 31 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:312066 BIOSIS
DOCUMENT NUMBER: PREV200100312066
TITLE: The **Notch ligand Jagged**-1 represents a novel growth factor of human hematopoietic stem cells.
AUTHOR(S): Karanu, F. N. (1); Murdoch, B. (1); Gallacher, L. (1); Wu, D. M. (1); Koremoto, M.; Sakano, S.; Bhatia, M. (1)
CORPORATE SOURCE: (1) Developmental Stem Cell Biology, The John P. Robarts Research Institute, London, ON Canada
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 680a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The **Notch ligand**, **Jagged**-1, plays an essential role in tissue formation during embryonic development of primitive organisms. However, little is known regarding the role of **Jagged**-1 in the regulation of tissue specific stem cells or its function in the human. Here, we show that uncommitted human hematopoietic cells and cells that comprise the putative blood stem cell microenvironment express **Jagged**-1 and the **Notch** receptors. Addition of a soluble form of human **Jagged**-1 to cultures of purified primitive human blood cells had modest effects in augmenting cytokine induced proliferation of progenitors. However, intravenous transplantation of cultured cells into immune deficient mice revealed that hJagged-1 induces the survival and expansion of human stem cells capable of pluripotent repopulating capacity. Our findings demonstrate that hJagged-1 represents a novel growth factor of human stem cells, thereby providing an opportunity for the clinical utility of **Notch ligands** in the expansion of primitive cells capable of hematopoietic reconstitution.

L8 ANSWER 32 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:452859 BIOSIS
DOCUMENT NUMBER: PREV200000452859
TITLE: JAGGED1 expression in human embryos: Correlation with the Alagille syndrome phenotype.
AUTHOR(S): Jones, E. A. (1); Clement-Jones, M.; Wilson, D. I.
CORPORATE SOURCE: (1) Institute of Human Genetics, School of Biochemistry and Genetics, University of Newcastle upon Tyne, Claremont Place, Ground Floor, Ridley Building, Newcastle upon Tyne, NE1 7RU UK
SOURCE: Journal of Medical Genetics, (September, 2000) Vol. 37, No. 9, pp. 658-662. print.
ISSN: 0022-2593.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Alagille syndrome (AGS, MIM 118450) is an autosomal dominant disorder with a variable phenotype characterised by hepatic, eye, cardiac, and skeletal

malformations and a characteristic facial appearance. Mutations within the gene JAGGED1 (JAG1), which encodes a ligand for NOTCH receptor(s), has been shown to cause Alagille syndrome. Interactions of NOTCH receptors and their ligands influence cell fate decisions in several developmental pathways. We report the tissue expression of JAG1 in human embryos. We have performed tissue in situ hybridisation on human embryos aged 32-52 days using 35S labelled riboprobes for JAG1. JAG1 is expressed in the distal cardiac outflow tract and pulmonary artery, major arteries portal vein, optic vesicle, otocyst, branchial arches, metanephros, pancreas, mesocardium, around the major bronchial branches, and in the neural tube. We conclude that JAG1 is expressed in the structures affected in Alagille syndrome, such as the pulmonary artery, anterior chamber of the eye, and face.

L8 ANSWER 33 OF 76 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 2000273831 MEDLINE
DOCUMENT NUMBER: 20273831 PubMed ID: 10812242
TITLE: Expression of notch receptors, notch ligands, and fringe genes in hematopoiesis.
AUTHOR: Singh N; Phillips R A; Iscove N N; Egan S E
CORPORATE SOURCE: Program in Cancer & Blood Research and, Toronto, Ontario, Canada.
SOURCE: EXPERIMENTAL HEMATOLOGY, (2000 May) 28 (5) 527-34. Journal code: EPR; 0402313. ISSN: 0301-472X.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000622
Last Updated on STN: 20000622
Entered Medline: 20000613

AB OBJECTIVE: Hematopoiesis is the process by which mature blood cell types are generated from a small population of pluripotent hematopoietic stem cells. How these cells undergo fate selection, however, is not fully understood. The **Notch** signaling system is known to mediate cell fate decisions of multipotent precursors in a wide range of complex animals throughout development. As **Notch** signaling involves cell-cell interactions, we sought to determine the expression of **Notch** receptors, **ligands**, and regulators in individual cell populations along the hematopoietic differentiation pathway. MATERIALS: Described here is a single cell RT-PCR analysis of Notch1, Notch3, Notch4, **Notch ligands** (Dll1 and Jagged1), and Fringe gene expression in cells of the blood system. As previously described, single cell globally amplified cDNA was generated by RT-PCR from various hematopoietic precursor cells whose potential was known from sibling analysis. A precursor hierarchy slot blot was created containing these cDNAs as well as samples from maturing blood cell populations and two fibroblast cell lines. The precursor slot blot was screened with probes for each of the candidate genes. RESULTS: Macrophage precursors expressed high levels of Notch1 transcript, while maturing macrophages expressed high levels of both Notch1 and Notch4. The **Jagged** 1 **ligand** transcript was highly expressed in terminally maturing cells including mast cells and megakaryocytes. In contrast, the Manic Fringe gene was highly expressed in uncommitted bi- and tri-potential precursors as well as in committed neutrophil and macrophage precursors. CONCLUSIONS: Distinct expression patterns of Jagged1 and Manic Fringe suggest that their corresponding proteins could regulate cell fate choices during hematopoiesis and may be responsible for regulating communication between lineage compartments during hematopoietic development.

L8 ANSWER 34 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:311830 BIOSIS
DOCUMENT NUMBER: PREV200100311830
TITLE: Primitive human hematopoietic cells transduced with a Lunatic Fringe expressing vector have increased numbers of CFU-C and LTC-IC, but not SRC when cultured on Jagged-1 expressing HS-27A stromal cell line.
AUTHOR(S): Ito, C. Y. (1); Gan, O. I. (1); Cohen, B. (1); Pereira, D. S.; Egan, S. (1); Dick, J. E. (1)
CORPORATE SOURCE: (1) Hospital For Sick Children, Toronto, ON Canada
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 492a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The interaction between **Notch** and its **ligands** plays an important role in regulating stem cell differentiation in many developmental systems, including hematopoesis. **Notch** 1 and 2 are expressed by primitive hematopoietic cells as well as by lymphoid and myeloid cells. Furthermore, the **Notch ligands** **Jagged**-1 and Delta-1 have been shown to inhibit the differentiation of hematopoietic progenitors. In addition to **ligand** binding, interaction with the Fringe proteins provides another level of regulation in **Notch** activation. However, little is known about Fringe function in hematopoiesis. Here, we show that endogenous Lunatic Fringe is mainly expressed in mature hematopoietic cells. We have investigated the role of Lunatic Fringe by constitutively expressing it in primitive human Lin- cells using a MSCV pac retrovirus vector and exposing the cells to the HS-27 a stromal line that expresses the **Notch ligand Jagged**-1. Retroviral overexpression of Lunatic Fringe alone did not affect CFU-C development as compared to Pac controls. However, when cells transduced with Lunatic Fringe were cultured at limiting dilution for 2.5 weeks on HS-27a cells there was a 2 fold increase in the number of CFU-C compared to the same cells cultured on HS-5 stromal cells that do not express **Jagged** -1. There was also a 2 fold increase in the number of CFU-C in Lunatic Fringe expressing cells compared to Pac infected control cells cultured on HS-27a cells. Likewise, there was a 3 fold increase in LTC-IC after the Lunatic Fringe infected cells were cultured at limiting dilution on HS-27a cells for 4.5 weeks when compared to the same cells cultured on HS-5 cells and a 3 fold increase in LTC-IC in Lunatic versus Pac transduced cells cultured on HS-27a cells. Interestingly, the number of CFU-C generated by these LTC-IC cultures was at least 8 fold greater than controls. By contrast, there was no increase in the number of SRC or the duration of SRC maintenance in the Lunatic Fringe expressing cells cultured on HS-27a for 2.5 weeks compared to control Pac transduced cells. Thus, Lunatic Fringe overexpression appears to influence **Jagged**-1 mediated signaling selectively in more committed CFU-C and LTC-IC progenitors

leading to their increased numbers, but may not affect the more primitive SRC. These studies suggest that Lunatic Fringe mediated **Notch** signaling plays an important role in regulating normal human hematopoiesis.

L8 ANSWER 35 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:225008 BIOSIS
DOCUMENT NUMBER: PREV200000225008
TITLE: Expression of Jagged/Notch family members in diverse tumors in vivo: Association in vitro with a transformed phenotype.
AUTHOR(S): Booth, Christina L. (1); Tenney, Callah H. (1); Sullivan, Margo B. (1); Lindner, Volkhard (1); Small, Deena (1); Prudovsky, Igor (1); Maciag, Thomas (1); Liaw, Lucy (1)
CORPORATE SOURCE: (1) Maine Med Ctr Res Institute, South Portland, ME USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 474-475. Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA April 01-05, 2000 ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 36 OF 76 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 2001052822 MEDLINE
DOCUMENT NUMBER: 20493260 PubMed ID: 11035934
TITLE: Isolation and characterization of the notch ligand delta4.
AUTHOR: Rao P K; Dorsch M; Chickering T; Zheng G; Jiang C; Goodearl A; Kadesch T; McCarthy S
CORPORATE SOURCE: Department of Genetics, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, 19104, USA.. kadesch@mail.med.upenn.edu
CONTRACT NUMBER: RO1 GM58228 (NIGMS)
T32 GM08216 (NIGMS)
SOURCE: EXPERIMENTAL CELL RESEARCH, (2000 Nov 1) 260 (2) 379-86. Journal code: EPB. ISSN: 0014-4827.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF253468; GENBANK-AF253469
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001212
AB **Notch** signaling plays a critical role in a variety of developmental programs. In vertebrates, the complexity of the process is underscored by the existence of multiple **Notch** receptors and multiple **ligands**, each of which displays a distinct expression profile. Furthermore, the **ligands** can be subdivided into two families, the Serrate/**Jagged** family and the Delta family. Here we present the isolation of a novel **Notch ligand**, Delta4. Expression analyses indicate that mouse Delta4 is highly expressed in the eye and lung during embryogenesis and in the heart, lung, liver, and kidney of the adult. Functionally, Delta4 is indistinguishable from Jagged1 in its abilities to inhibit myogenesis and to stimulate transcription through Notch1 and the DNA binding protein CSL. Copyright 2000 Academic Press.

L8 ANSWER 37 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:322046 BIOSIS
DOCUMENT NUMBER: PREV200100322046
TITLE: The presence of soluble **Notch ligand**, **Jagged**-1 (but not Delta-1), improves survival and donor engraftment in a murine transplantation model using ex vivo-expanded marrow cells.
AUTHOR(S): von Drygalski, Annette (1); Savatski, Laura L. (1); Koremoto, Masahide; Sakano, Seiji; Adamson, John W. (1)
CORPORATE SOURCE: (1) Blood Research Institute, Blood Center of Southeastern Wisconsin, Milwaukee, WI USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 372a. print. Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology . ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Ex vivo expansion of hematopoietic stem cells (HSC) could be critical with grafts known to have low HSC numbers if the expansion process did not impair the long-term marrow reconstitution capacity of the HSC. The **Notch** family of cell membrane-bound **ligands** may allow HSC to remain uncommitted during the expansion of more differentiated progenitor cells. To investigate this, the effects of two **Notch** -1 family **ligands** - **Jagged**-1 and Delta-1 - were studied by adding them to cultures of C57B1-6J (CD45.1) bone marrow (BM) light-density (LD) cells in the presence of thrombopoietin, Interleukin-11, Stem Cell Factor and Flt-3 **ligand**. With cytokines alone, a 6.7-fold (n=2; 5.9 and 7.4-fold) expansion in total cell numbers was achieved by day 6. In the presence of the same four cytokines, and with **Jagged** coated on the surface of the culture plates, expansion was reduced to 4.4-fold (3.8 and 5.0-fold). With Delta bound to the plates, expansion was 4.7-fold (3.9 and 5.5-fold). We then examined survival and percent donor engraftment by transplanting 2X104 unmanipulated BM LD cells, as controls, or the progeny from the original cell number expanded for 6 days with cytokines or cytokines to which **Jagged** or Delta were added, into lethally-irradiated (9 Gy) congenic recipients (CD45.2; 27 mice/group; 2 experiments). Survival of controls at 8 weeks was 92%, with 72.7% donor engraftment (SEM=26.1%). Survival of mice transplanted with cells expanded in cytokines alone was 25% with a mean donor engraftment of 15.1% (SEM=16.8%) at 9 weeks. The survival of mice transplanted with cells expanded in the presence of **Jagged** or Delta was 67% and 50%, respectively, with a mean donor engraftment of 29.6% (SEM=16.8%) and 9.5% (SEM=9.4%). Statistical analysis showed a significantly improved percent survival at day 60 for those animals receiving cells exposed to **Jagged** (p=0.02) and, to a lesser extent, to Delta (p=0.15). Log-rank analysis of the differences in percent survival throughout the entire 60 day testing period gave a value of p=0.04 for **Jagged** and p=0.16 for Delta. These results provide evidence that strategies designed to limit the differentiation of HSC, while expanding progenitor cell numbers in the presence of various

cytokines - in this case by using **Notch ligands** - result in greater retention of HSC capable of radioprotection and long-term marrow reconstitution.

L8 ANSWER 38 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:311665 BIOSIS
DOCUMENT NUMBER: PREV200100311665
TITLE: Notch signalling via RBP-J reduces self renewal of multipotent hematopoietic progenitor cells and promotes differentiation into granulocytes, macrophages and erythroid cells.
AUTHOR(S): Just, Ursula (1); Schroeder, Timm (1)
CORPORATE SOURCE: (1) Institute of Clinical Molecular Biology, GSF-National Research Centre for Environment and Health, Munich Germany
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 286a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology . ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Notch** receptors are involved in the regulation of cell fate decisions, differentiation and proliferation in many developmental systems. To date, four different mammalian **Notch** receptors have been described. The **ligands** are also transmembrane proteins and include **Jagged**-1 and -2, and Delta-like -1, -3, -4. After **ligand** binding and activation, the **Notch** intracellular domain (NIC) is released from the cytoplasmic membrane. NIC then translocates to the nucleus where it binds to the transcriptional repressor RBP-J, thereby converting RBP-J into a transcriptional activator. The expression of **Notch** on hematopoietic cells and of cognate **Notch ligands** on bone marrow stromal cells suggest a role for **Notch** signalling in the regulation of hematopoiesis. Recently, we have shown that activated mNotch1 promotes granulocytic differentiation of the myeloid progenitor cell line 32D (EMBO J 19, 2558-2568, 2000). To investigate the consequences of mNotch1 signalling in multipotent progenitor cells, multipotent progenitor FDCP-mix cell lines were engineered to permit the conditional induction of the constitutively active intracellular domain of mNotch1 (mN1IC) by the 4-hydroxytamoxifen-inducible system. Under conditions that promote self renewal of FDCP-mix cells, i.e. in the presence of high amounts of IL-3, the induction of mN1IC activity resulted in a decrease in self renewal and increased myeloid differentiation of FDCP-mix cells. In the presence of hematopoietic cytokines such as GM-CSF and erythropoietin that support differentiation of FDCP-mix cells, the induction of mN1IC led to an accelerated and increased differentiation along the granulocyte, macrophage, and erythrocyte lineage. Expression of a transcriptionally active derivative of RBP-J (RBP-J-VP16) also increased myeloid differentiation. To further test the role of **Notch** signalling in a physiological context, FDCP-mix cells were cultured on fibroblast layers that expressed or did not express the **Notch ligand** Jagged1. Similar to the induction of mN1IC, Jagged1 accelerated myeloid differentiation of FDCP-mix cells. Taken together, our results suggest that activation of mNotch1 signalling reduces self renewal of multipotent progenitor cells and induces differentiation into granulocytes, macrophages and erythroid cells.

L8 ANSWER 39 OF 76 MEDLINE DUPLICATE 19
ACCESSION NUMBER: 2001447933 MEDLINE
DOCUMENT NUMBER: 21198764 PubMed ID: 11303783
TITLE: Requirement for presenilin 1 in facilitating lagged 2-mediated endoproteolysis and signaling of notch 1.
AUTHOR: Martys-Zage J L; Kim S H; Berechid B; Bingham S J; Chu S; Sklar J; Nye J; Sisodia S S
CORPORATE SOURCE: Department of Neurobiology, Pharmacology, and Physiology, Howard Hughes Medical Institute, The University of Chicago, IL 60637, USA.
CONTRACT NUMBER: 1PO1 AG14248 (NIA)
SOURCE: JOURNAL OF MOLECULAR NEUROSCIENCE, (2000 Dec) 15 (3) 189-204.
Journal code: AVM; 9002991. ISSN: 0895-8696.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20010813
Entered Medline: 20010809
AB Presenilin 1 (PS1), a polytopic membrane protein, is required for endoproteolytic processing at gamma-secretase site within the transmembrane domain of amyloid precursor proteins (APP). In addition, PS1 and its orthologues facilitate signaling of **Notch** family members, cell-surface receptors that specify cell fates during development. To clarify the mechanism(s) by which PS facilitates **Notch** signaling, we examined human **Jagged**-2-dependent metabolism and activity of a chimeric full-length Notch1-GFP molecule expressed in fibroblasts with heterozygous, or homozygous deletions of PS1. We demonstrate that PS1 is required for facilitating **Jagged** 2-mediated proteolysis and that translocation and accumulation of NICD in the nucleus correlates with signaling activity. Moreover, in a **ligand**-independent, Ca2+-depletion paradigm, we demonstrate that PS1 facilitates endoproteolysis of a plasma-membrane-associated, Notch1-GFP derivative. Finally, we report that NICD production is inhibited by L-685,458, a potent and selective inhibitor that blocks solubilized gamma-secretase activity and Abeta production in cultured cells. These findings strongly suggest that intramembranous processing of APP and **Notch** 1 are mediated by similar, if not identical, proteases that require PS1 for their activation.

L8 ANSWER 40 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:419421 BIOSIS
DOCUMENT NUMBER: PREV200000419421
TITLE: Notch ligands prohibit terminal differentiation of human osteoclast precursors.
AUTHOR(S): Iwai, S. (1); Takahashi, N.; Udagawa, N.; Nakahata, T.; Suda, T.; Shibuya, M. (1)
CORPORATE SOURCE: (1) Department of Genetics, The Institute of Medical Science, Tokyo University, Tokyo Japan
SOURCE: Journal of Bone and Mineral Research, (September, 2000) Vol. 15, No. Suppl. 1, pp. S183. print.

Meeting Info.: Twenty-Second Annual Meeting of the American Society for Bone and Mineral Research Toronto, Ontario, Canada September 22-26, 2000 American Society for Bone and Mineral Research
. ISSN: 0884-0431.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 41 OF 76 MEDLINE DUPLICATE 20
ACCESSION NUMBER: 2001040703 MEDLINE
DOCUMENT NUMBER: 20386733 PubMed ID: 10933602
TITLE: Microenvironmental influences on human B-cell development.
COMMENT: Erratum in: Immunol Rev 2000 Dec;178:186
AUTHOR: Bertrand F E; Eckfeldt C E; Fink J R; Lysholm A S; Pribyl J A; Shah N; LeBien T W
CORPORATE SOURCE: University of Minnesota Cancer Center, Minneapolis 55455, USA.
CONTRACT NUMBER: R01 CA31685 (NCI)
R01 CA76055 (NCI)
T32 AI07313 (NIAID)
SOURCE: IMMUNOLOGICAL REVIEWS, (2000 Jun) 175 175-86. Ref: 72
Journal code: GG4; 7702118. ISSN: 0105-2896.
PUB. COUNTRY: Denmark
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010918
Entered Medline: 20001207
AB Mammalian B-cell development can be viewed as a developmental performance with several acts. The acts are represented by checkpoints centered around commitment to the B-lineage and functional Ig gene rearrangement--culminating in expression of the pre-B-cell receptor (pre-BCR) and the BCR. Progression of cells through these checkpoints is profoundly influenced by the fetal liver and adult bone marrow (BM) stromal cell microenvironments. Our laboratory has developed a model of human B-cell development that utilizes freshly isolated/non-transformed human BM stromal cells as an in vitro microenvironment. Human CD34+ hematopoietic stem cells plated in this human BM stromal cell microenvironment commit to the B lineage and progress through the pre-BCR and BCR checkpoints. This human BM stromal cell microenvironment also provides survival signals that prevent apoptosis in human B-lineage cells. Human B-lineage cells exhibit differential expression of **Notch** receptors and human BM stromal cells express the **Notch ligand Jagged**-1. These results suggest a potential role for **Notch** in regulating B-lineage commitment and/or progression through the pre-BCR and BCR checkpoints.

L8 ANSWER 42 OF 76 MEDLINE DUPLICATE 21
ACCESSION NUMBER: 2001033947 MEDLINE
DOCUMENT NUMBER: 20424590 PubMed ID: 10975791
TITLE: Advances in familial and congenital cholestatic diseases. Clinical and diagnostic implications.
AUTHOR: Colombo C; Okolicsanyi L; Strazzabosco M
CORPORATE SOURCE: Department of Paediatrics, University of Sassari, Italy.
SOURCE: DIGESTIVE AND LIVER DISEASE, (2000 Mar) 32 (2) 152-9. Ref: 45
Journal code: DQK.
PUB. COUNTRY: Italy
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001130
AB Recent progress in liver cell biology and molecular genetics revealed that a number of familial and congenital cholestatic disorders are caused by mutations in genes coding for hepatobiliary-transporter or for signalling proteins involved in morphogenesis. The status of the field is reviewed in the light of its impact on current diagnostic and clinical practice. The heterogeneous progressive familial intrahepatic cholestasis can now be separated into different genetic diseases. FIC1-defective progressive familial intrahepatic cholestasis (previously Byler disease) is determined by mutations in the FIC1 gene, coding for P-type ATPases of unknown physiological function, while a second form (bile salt export pump defective progressive familial intrahepatic cholestatis) is caused by a defective function of the canalicular bile salt export pump. Furthermore, a group of progressive familial intrahepatic cholestasis patients with high serum gamma glutamyltranspeptidase have mutations in the gene (PGY3) coding for the MDR3 protein, a canalicular ATP-dependent phopshatidylcholine translocator. Recurrent intrahepatic cholestasis (previously benign recurrent cholestasis), is also linked to specific mutations in the FIC1 gene. Finally, in Alagille syndrome, mutations in the JAG1 gene cause deficiency **Jagged** 1, a **ligand** for **Notch** 1, a receptor determining cell fate during early embryogenesis. Diagnosis of Alagille syndrome, a condition that should be suspected in all patients with unexplained cholestasis, will thus be confirmed by genetic analysis for mutations of JAG1. In children with cholestasis and low serum bile acid levels, an inborn error of bile acid synthesis should be excluded by urinary bile acid analysis by means of fast atom bombardment-ionization mass-spectrometry. In contrast, in children with cholestasis and high serum bile acid concentrations, a high serum gamma glutamyltranspeptidase value would indicate MDR3 deficiency, which should be excluded through biliary phospholipid determination and genetic analysis of PGY3 gene. Finally, in those children with cholestasis, high serum bile acids and low gamma glutamyltranspeptidase activity, analysis of mutation in FIC1 and bile salt export pump genes may lead to the diagnosis of progressive familial intrahepatic cholestasis either from bile salt export pump or FIC1 deficiency.

L8 ANSWER 43 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:299233 BIOSIS
DOCUMENT NUMBER: PREV200100299233
TITLE: mNotch1 signalling reduces proliferation of myeloid progenitor cells by altering cell cycle kinetics.
AUTHOR(S): Just, Ursula (1); Schroeder, Timm (1)

CORPORATE SOURCE: (1) Institute of Clinical Molecular Biology, GSF-National Research Centre for Environment and Health, Munich Germany
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 145b. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Notch** receptors are involved in the regulation of cell fate decisions, differentiation and proliferation in many tissues. To date, four different mammalian **Notch** receptors have been described. The **ligands** are also transmembrane proteins and include **Jagged**-1 and -2, and Delta-like -1, -2, -3. After **ligand** binding and activation, the **Notch** intracellular domain (NIC) is released from the cytoplasmic membrane. NIC then translocates to the nucleus where it binds to the transcriptional repressor RBP-J, thereby converting RBP-J into a transcriptional activator. The expression of **Notch** receptors on haemopoietic cells and of cognate **ligands** on bone marrow stromal cells suggests a possible role for **Notch** signalling in the regulation of haemopoiesis. Using 32D myeloid progenitor cell lines engineered to permit the conditional induction of the constitutively active intracellular domain of mNotch1 (mN1IC) by the 4-hydroxytamoxifen(OHT)-inducible system (rNERTneo32D), we have recently shown that mNotch1 signalling via RBP-J promotes granulocytic differentiation of myeloid progenitor cells (EMBO J 19, 2558-2568, 2000). To assess the involvement of Notch1 signalling on cell proliferation of myeloid progenitor cells, proliferation, cell cycle status and apoptosis of rNERTneo32D cell lines were analysed in the presence or absence of OHT. The induction of mN1IC by OHT resulted in reduction of proliferation ($p<0.01$) and accumulation of cells in the G1/G0 phase of the cell cycle ($p<0.001$) without substantially affecting apoptosis of 32D cells. These effects were observed under culture conditions that allow differentiation and, to a lesser degree, under conditions which normally promote self-renewal in the absence of differentiated cells. Our data suggest that mNotch1 signalling suppresses proliferation of myeloid progenitor cells by altering cell cycle kinetics.

L8 ANSWER 44 OF 76 MEDLINE DUPLICATE 22
ACCESSION NUMBER: 2000133382 MEDLINE
DOCUMENT NUMBER: 20133382 PubMed ID: 10668203
TITLE: The role of the epidermal growth factor-like protein dlk in cell differentiation.
AUTHOR: Laborda J
CORPORATE SOURCE: Laboratory of Immunobiology, Center for Biologics Evaluation and Research, Rockville, MD, USA.. jlaborda@med-ab.uclm.es
SOURCE: HISTOLOGY AND HISTOPATHOLOGY, (2000 Jan) 15 (1) 119-29. Ref: 40
Journal code: BEM; 8609357. ISSN: 0213-3911.
PUB. COUNTRY: Spain
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000229
AB This review focuses on the current knowledge about the function of the EGF-like homeotic protein dlk. dlk is a transmembrane protein that possesses six Epidermal Growth Factor-like sequences at the extracellular domain, a single transmembrane domain and a short intracellular tail. Because of its overall structure and amino acid homology, dlk belongs to the EGF-like homeotic protein family. This family includes proteins such as the **Notch** receptor and its homologues, as well as **Notch ligands**, such as Delta, Serrate, and their mammalian homologues Dll1, Dll2 and Dll3 and **Jagged** 1 and **Jagged** 2. (For a recent review see Fleming, 1998). dlk is highly expressed by preadipose cell lines, and neuroendocrine tumors, such as pheochromocytomas and neuroblastomas. dlk has been involved in several differentiation processes, such as adipogenesis, hematopoiesis and B cell lymphopoiesis, and neuroendocrine differentiation, including the differentiation of pancreas and the adrenal gland. The extracellular region of dlk can be released by action of an unknown protease and this soluble dlk variant accumulates in the amniotic fluid and is able to inhibit adipocyte differentiation in vitro. Recent evidence indicates, however, that membrane-associated dlk variants play a positive role in the differentiation process. These findings suggest that dlk plays an important role in differentiation and tumorigenesis of several cellular types.

L8 ANSWER 45 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:82827 BIOSIS
DOCUMENT NUMBER: PREV200100082827
TITLE: Role of the jagged/notch gene family in T-cell activation versus anergy.
AUTHOR(S): Ponchel, Frederique (1); Ali, Manir (1); Verhoef, Adrienne (1); Lamb, Jonathan (1); Isaacs, John (1)
CORPORATE SOURCE: (1) Molecular Medicine Unit, University of Leeds, Leeds UK
SOURCE: Immunology, (December, 2000) Vol. 101, No. Supplement 1, pp. 8. print.
Meeting Info.: Annual Congress of the British Society for Immunology Harrogate, UK December 05-08, 2000 British Society for Immunology
. ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 46 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:68694 BIOSIS
DOCUMENT NUMBER: PREV200100068694
TITLE: Angiotensin II (Ang II) inhibits the expression of the Notch signaling pathway in vascular smooth muscle cells (VSMC): Mediator role of ERK.
AUTHOR(S): Campos, Alexandre H. (1); Pollman, Matthew J. (1); Gibbons, Gary H. (1)
CORPORATE SOURCE: (1) Morehouse CV Research Inst, Atlanta, GA USA
SOURCE: Circulation, (October 31, 2000) Vol. 102, No. 18

Supplement, pp. II.40-II.41. print.
Meeting Info.: Abstracts from Scientific Sessions 2000 New Orleans, Louisiana, USA November 12-15, 2000
ISSN: 0009-7322.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 47 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:134464 BIOSIS
DOCUMENT NUMBER: PREV200100134464
TITLE: Glial expression of Notch receptors and their ligands in the postnatal rodent cerebellum.
AUTHOR(S): Tanaka, M. (1); Marunouchi, T.
CORPORATE SOURCE: (1) Fujita Hlth Univ, Toyoake, Aichi Japan
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-791.8. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000
Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Notch** family molecules were thought to be negative regulators of neuronal differentiation in early brain development. After a widespread expression in the embryonic brain, **Notch** continues to be expressed in the specific regions such as the cerebellum and hippocampus in the postnatal brain of rodents. Using lacZ-knockin mice into the Notch2 locus, we recently found that Notch2 is expressed by radial glia in the postnatal cerebellum and hippocampus and by astrocytes in dissociated cell cultures (J. Neurobiol. 41:524-539, 1999). Cerebellar and hippocampal radial glia are regarded as being a unique immature stage in glial differentiation because they postnatally maintain vimentin expression and proliferative activity. As the next step for investigating the roles of **Notch** signaling in the postnatal brain, we immunohistochemically examined the expression patterns of **Notch** receptors (Notch1-3) and their **ligands** (Delta, **Jagged**) in the postnatal cerebellum of rats and mice in the present study. The strongest expression of Notch1-3 and Jagged2 was observed in the radial processes and the cell bodies of Bergmann glia, the cerebellar radial glia. Thus, Bergmann glia could interact each other through the intercellular Jagged2-**Notch** signaling during cerebellar development. In addition, some of the activated astrocytes in vitro expressed **Notch**, whereas normal astrocytes in vivo showed a weak or no expression of **Notch**. These findings, together with our previous ones, suggest that **Notch** signaling has roles in the specific class of glial cells (radial glia) and in the specific states of glial cells (immature glia and activated astrocytes).

L8 ANSWER 48 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:97069 BIOSIS
DOCUMENT NUMBER: PREV200100097069
TITLE: Independent effects of presenilin 1 on jagged 2-mediated signaling and proteolysis of Notch 1.
AUTHOR(S): Martys-Zage, J. (1); Berechid, B. E.; Nye, J. S.; Sklar, J.; Thinakaran, G.; Kim, S. H.; Sisodia, S. S.
CORPORATE SOURCE: (1) Univ of Chicago, Chicago, IL USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-298.4. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000
Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Mutations in the gene encoding Presenilin 1 (PS1), cosegregate with the vast majority of pedigrees with autosomal dominant, familial Alzheimer's disease. Loss-of-function analyses have supported a role for PS1 in facilitating signaling of **Notch** 1, and biochemical studies have shown that PS1 facilitates proteolysis of constitutively-active **Notch** 1 species. To examine the **ligand**-dependent proteolysis of full-length **Notch** 1 and signaling, we stably expressed cDNA encoding full-length **Notch** 1 with a C-terminal GFP tag in PS1+/- and PS1-/- fibroblasts. These cell lines were cocultured with mouse 3T3 cells expressing the **Notch ligand**, **Jagged** 2. We show that while furin and TACE processing of the **Notch**-GFP chimera occurs to similar extents in PS1+/- and PS1-/- cells, the levels of the **Notch** 1 intracellular domain (NICD) are reduced in PS1 -/- cells. Moreover, in PS1-/- cells, the NICD is largely excluded from the nucleus and **Jagged** 2-mediated activation of a HES-1 reporter gene is markedly reduced. These studies are the first to document that PS1 plays a role in **ligand**-mediated intramembranous processing of **Notch** 1. Ongoing studies are focused on assessing the activity of "gamma-secretase" inhibitors in NICD production and on obtaining real-time images of **Notch** 1 distribution and proteolysis in PS1+/- and PS1-/- fibroblasts and primary neurons.

L8 ANSWER 49 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:92474 BIOSIS
DOCUMENT NUMBER: PREV200100092474
TITLE: Activation of notch-1 receptor by jagged-1 in oligodendrocyte progenitors inhibits myelination of cerebellar parallel fibers.
AUTHOR(S): Bongarzone, E. R. (1); Givogri, M. I.; Costa, M. R.; Schonmann, V.; Howard, S.; Silva, A.; Campagnoni, A. T.
CORPORATE SOURCE: (1) UCLA Medical School, Neuropsychiatric Institute, Los Angeles, CA USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-515.1. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000
Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Activation of the **notch**-1 receptor by **jagged**-1, its natural **ligand**, is known to inhibit oligodendrocyte (OL) differentiation and subsequent myelination in the optic nerve. We have tested the hypothesis that the occurrence of unmyelinated axons in the

cerebellar molecular layer might be due, at least in part, to inhibition of OL differentiation via the **notch**-1/**jagged**-1 pathway in this region. Cerebellar OL progenitor cells (OPCs) and cerebellar granule cells were found to express the **notch**-1 receptor in vivo and in vitro by several methods, including RT-PCR, immunofluorescent confocal microscopy and Western blot analysis. Interestingly, in cultured OLs the intracellular localization of the **notch**-1 receptor was influenced by the differentiation state of the cell. For example, in OPCs the receptor localized to specific sectors within the cell bodies, in contrast to differentiated OLs where it was more homogeneously distributed throughout the cell bodies and processes. Expression of **jagged**-1, the natural **ligand** of the **notch**-1 receptor, was examined during cerebellar development. Purkinje cells did not express detectable levels of **jagged**-1 in the developmental period during which their axons became myelinated. However, the unmyelinated parallel fibers of the molecular layer exhibited **jagged**-1 immunoreactivity during and well after the peak of myelination, suggesting that expression of **jagged**-1 might block OPCs in this region from maturing into myelinating OLs. To test this hypothesis, we examined the extent of myelination in the cerebellum of heterozygous, P35 knock-out mice carrying a disruption of the **notch**-1 gene. Immunohistochemical analysis revealed the presence of numerous MBP+ ascending fibers in the molecular layer of the cerebella of these mice. In contrast, control litter mates showed a complete absence of immunoreactivity of this myelin marker in the cerebellar molecular layer. These findings support the notion that mechanisms of lateral inhibition triggered by the **notch**-signaling pathway in OPCs might actively participate in the timing of OL differentiation and whether or not axons become myelinated in the developing brain.

L8 ANSWER 50 OF 76 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:795994 CAPLUS
DOCUMENT NUMBER: 132:31744
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Ltd., UK
SOURCE: PCT Int. Appl., 745 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964627	A2	19991216	WO 1999-GB1780	19990604

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

GB 1998-12099	A	19980606
GB 1998-13291	A	19980620
GB 1998-13611	A	19980624
GB 1998-13835	A	19980627
GB 1998-14110	A	19980701
GB 1998-14580	A	19980707
GB 1998-15438	A	19980716
GB 1998-15574	A	19980718
GB 1998-15576	A	19980718
GB 1998-16085	A	19980724
GB 1998-16086	A	19980724
GB 1998-16921	A	19980805
GB 1998-17097	A	19980807
GB 1998-17200	A	19980808
GB 1998-17632	A	19980814
GB 1998-17943	A	19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic.RTM." profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L8 ANSWER 51 OF 76 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:795993 CAPLUS
DOCUMENT NUMBER: 132:31743
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Limited, UK
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964626	A2	19991216	WO 1999-GB1779	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9941586	A1	19991230	AU 1999-41586	19990604
AU 9941587	A1	19991230	AU 1999-41587	19990604
GB 2339200	A1	20000119	GB 1999-12914	19990604
GB 2339200	B2	20010912		
EP 1084273	A1	20010321	EP 1999-925207	19990604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:	GB 1998-12098	A	19980606
	GB 1998-28289	A	19981223
	GB 1998-16086	A	19980724
	GB 1998-16921	A	19980805
	GB 1998-17097	A	19980807
	GB 1998-17200	A	19980808
	GB 1998-17632	A	19980814
	GB 1998-17943	A	19980819
	WO 1999-GB1779	W	19990604

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

L8 ANSWER 52 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER:	2000:210379 BIOSIS
DOCUMENT NUMBER:	PREV200000210379
TITLE:	Potential mechanisms regulating the differentiation of neuroepithelial stem cells.
AUTHOR(S):	Galloway, D. C. (1); Mellodew, K. L. (1); Price, J. (1)
CORPORATE SOURCE:	(1) Institute of Psychiatry, ReNeuron, Denmark Hill, London, SE5 8AF UK
SOURCE:	Society for Neuroscience Abstracts, (1999) Vol. 25, No. 1-2, pp. 1766. Meeting Info.: 29th Annual Meeting of the Society for Neuroscience. Miami Beach, Florida, USA October 23-28, 1999 Society for Neuroscience . ISSN: 0190-5295.
DOCUMENT TYPE:	Conference
LANGUAGE:	English
SUMMARY LANGUAGE:	English

L8 ANSWER 53 OF 76 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1999:203672 CAPLUS
DOCUMENT NUMBER:	131:57123
TITLE:	Human ligands of the Notch receptor
AUTHOR(S):	Gray, Grace E.; Mann, Robert S.; Mitsiadis, Efthimios; Henrique, Domingos; Carcangiu, Maria-Louisa; Banks, Amy; Leiman, John; Ward, David; Ish-Horowitz, David; Artavanis-Tsakonas, Spyros
CORPORATE SOURCE:	Department of Cell Biology, Yale University School of Medicine, New Haven, CT, USA
SOURCE:	Am. J. Pathol. (1999), 154(3), 785-794 CODEN: AJPAA4; ISSN: 0002-9440
PUBLISHER:	American Society for Investigative Pathology
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB During development, the Notch signaling pathway is essential for the appropriate differentiation of many cell types in organisms across the phylogenetic scale, including humans. Notch signaling is also implicated in human diseases, including a leukemia and two hereditary syndromes known as Alagille and CADASIL. To generate tools for pursuing the role of the Notch pathway in human disease and development, the authors have cloned and analyzed the expression of three human homologs of the Notch ligands Delta and Serrate, human Jagged1 (HJ1), human Jagged2 (HJ2), and human Delta1 (H-Delta-1), and detd. their chromosomal localizations. The authors have also raised antibodies to HJ1, and used these antibodies in conjunction with in situ hybridization to examine the expression of these ligands in normal and cancerous cervical tissue. The authors find that, as reported previously for Notch, the ligands are up-regulated in certain neoplastic tissues. This observation is consistent with the notion that Notch signaling is an important element in these pathogenic conditions, raising the possibility that modulation of Notch activity could be used to influence the fate of the cells and offering a conceivable therapeutic avenue.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 54 OF 76 MEDLINE DUPLICATE 23

ACCESSION NUMBER:	2000004539 MEDLINE
DOCUMENT NUMBER:	20004539 PubMed ID: 10533065
TITLE:	Jagged-1 mutation analysis in Italian Alagille syndrome patients.
AUTHOR:	Pilia G; Uda M; Macis D; Frau F; Crisponi L; Balli F; Barbera C; Colombo C; Frediani T; Gatti R; Iorio R; Marazzi M G; Marcellini M; Musumeci S; Nebbia G; Vajro P; Ruffa G; Zancan L; Cao A; DeVirgilis S
CORPORATE SOURCE:	Istituto di Ricerca sulle Talassemie ed Anemie Mediterranee CNR, Cagliari, Italy.. pilia@vaxca1.unica.it

SOURCE: HUMAN MUTATION, (1999) 14 (5) 394-400.
Journal code: BRD; 9215429. ISSN: 1059-7794.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000106

AB Alagille syndrome (AGS) is an autosomal dominant disorder with developmental abnormalities affecting the liver, heart, eyes, vertebrae, and craniofacial region. The **Jagged**-1 (JAG1) gene, which encodes a **ligand** of **Notch**, has recently been found mutated in AGS. In this study, mutation analysis of the JAG1 gene performed on 20 Italian AGS patients led to the identification of 15 different JAG1 mutations, including a large deletion of the 20p12 region, six frameshift, three nonsense, three splice-site, and two missense mutations. The two novel missense mutations were clustered in the 5' region, while the remaining mutations were scattered throughout the gene. The spectrum of mutations in Italian patients was similar to that previously reported. We also studied in detail a complex splice site mutation, 3332dup18bp, which was shown to lead to an abnormal JAG1 mRNA, resulting in a premature stop codon. With the exception of the missense mutations, the majority of the JAG1 mutations are therefore likely to produce truncated proteins. Since the phenotype of the patient with a complete deletion of the JAG1 gene is indistinguishable from that of patients with intragenic mutations, our study further supports the hypothesis that haploinsufficiency is the most common mechanism involved in AGS pathogenesis. Furthermore, our data confirmed the absence of a correlation between the genotype of the JAG1 gene and the AGS phenotype.

L8 ANSWER 55 OF 76 MEDLINE DUPLICATE 24
ACCESSION NUMBER: 1999178266 MEDLINE
DOCUMENT NUMBER: 99178266 PubMed ID: 10080181
TITLE: Notch signalling pathway mediates hair cell development in mammalian cochlea.
COMMENT: Comment in: Nat Genet. 1999 Mar;21(3):253-4
AUTHOR: Lanford P J; Lan Y; Jiang R; Lindsell C; Weinmaster G; Gridley T; Kelley M W
CORPORATE SOURCE: Department of Cell Biology, Georgetown University School of Medicine, Washington, DC 20007, USA.
CONTRACT NUMBER: K02
SOURCE: NATURE GENETICS, (1999 Mar) 21 (3) 289-92.
Journal code: BRO; 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990413
Last Updated on STN: 19990413
Entered Medline: 19990331

AB The mammalian cochlea contains an invariant mosaic of sensory hair cells and non-sensory supporting cells reminiscent of invertebrate structures such as the compound eye in Drosophila melanogaster. The sensory epithelium in the mammalian cochlea (the organ of Corti) contains four rows of mechanosensory hair cells: a single row of inner hair cells and three rows of outer hair cells. Each hair cell is separated from the next by an interceding supporting cell, forming an invariant and alternating mosaic that extends the length of the cochlear duct. Previous results suggest that determination of cell fates in the cochlear mosaic occurs via inhibitory interactions between adjacent progenitor cells (lateral inhibition). Cells populating the cochlear epithelium appear to constitute a developmental equivalence group in which developing hair cells suppress differentiation in their immediate neighbours through lateral inhibition. These interactions may be mediated through the **Notch** signalling pathway, a molecular mechanism that is involved in the determination of a variety of cell fates. Here we show that genes encoding the receptor protein Notch1 and its **ligand**, **Jagged** 2, are expressed in alternating cell types in the developing sensory epithelium. In addition, genetic deletion of Jag2 results in a significant increase in sensory hair cells, presumably as a result of a decrease in **Notch** activation. These results provide direct evidence for **Notch** -mediated lateral inhibition in a mammalian system and support a role for **Notch** in the development of the cochlear mosaic.

L8 ANSWER 56 OF 76 BIOSIS
ACCESSION NUMBER: 1999:438261 BIOSIS
DOCUMENT NUMBER: PREV199900438261
TITLE: Stimulation of osteoblast differentiation and bone formation in vitro and in vivo by Notch receptor-ligand interactions.
AUTHOR(S): Dallas, D. J. (1); Birch, M. A.; Peet, N. M.; Murphy, G. (1); Skerry, T. M.
CORPORATE SOURCE: (1) Biological Sciences, University of East Anglia, Norwich, Norfolk UK
SOURCE: Journal of Bone and Mineral Research, (Sept., 1999) Vol. 14, No. SUPPL. 1, pp. S172.
Meeting Info.: Twenty-First Annual Meeting of the American Society for Bone and Mineral Research St. Louis, Missouri, USA September 30-October 4, 1999 American Society for Bone and Mineral Research
. ISSN: 0884-0431.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 57 OF 76 BIOSIS
ACCESSION NUMBER: 2000:38710 BIOSIS
DOCUMENT NUMBER: PREV200000038710
TITLE: A non-transmembrane form of the **Notch** **ligand**, **Jagged**-1, regulates the formation of matrix-dependent chord-like structures in NIH 3T3 cells.
AUTHOR(S): Small, Deena (1); Prudovsky, Igor (1); Wong, Michael; Booth, Christina (1); Liaw, Lucy (1); Vary, Calvin (1); Maciag, Thomas (1)
CORPORATE SOURCE: (1) Maine Medical Center Research Institute, 125 John Roberts Rd., South Portland, ME, 04106 USA
SOURCE: Molecular Biology of the Cell, (Nov., 1999) Vol. 10, No. SUPPL., pp. 37a.
Meeting Info.: 39th Annual Meeting of the American Society for Cell Biology Washington, D.C., USA December 11-15, 1999

The American Society for Cell Biology
. ISSN: 1059-1524.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 58 OF 76 MEDLINE DUPLICATE 25
ACCESSION NUMBER: 1998374257 MEDLINE
DOCUMENT NUMBER: 98374257 PubMed ID: 9707552
TITLE: PDZ-domain-mediated interaction of the Eph-related receptor tyrosine kinase EphB3 and the ras-binding protein AF6 depends on the kinase activity of the receptor.
AUTHOR: Hock B; Bohme B; Karn T; Yamamoto T; Kaibuchi K; Holtrich U; Holland S; Pawson T; Rubsamen-Waigmann H; Strebhardt K
CORPORATE SOURCE: Chemotherapeutisches Forschungsinstitut, Georg-Speyer-Haus, Paul-Ehrlich-Strasse 42-44, 60596 Frankfurt, Germany.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Aug 18) 95 (17) 9779-84. Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980925
Last Updated on STN: 20000303
Entered Medline: 19980917

AB Eph-related receptor tyrosine kinases (RTKs) have been implicated in intercellular communication during embryonic development. To elucidate their signal transduction pathways, we applied the yeast two-hybrid system. We could demonstrate that the carboxyl termini of the Eph-related RTKs EphA7, EphB2, EphB3, EphB5, and EphB6 interact with the PDZ domain of the ras-binding protein AF6. A mutational analysis revealed that six C-terminal residues of the receptors are involved in binding to the PDZ domain of AF6 in a sequence-specific fashion. Moreover, this PDZ domain also interacts with C-terminal sequences derived from other transmembrane receptors such as neurexins and the **Notch ligand Jagged**. In contrast to the association of EphB3 to the PDZ domain of AF6, the interaction with full-length AF6 clearly depends on the kinase activity of EphB3, suggesting a regulated mechanism for the PDZ-domain-mediated interaction. These data gave rise to the idea that the binding of AF6 to EphB3 occurs in a cooperative fashion because of synergistic effects involving different epitopes of both proteins. Moreover, in NIH 3T3 and NG108 cells endogenous AF6 is phosphorylated specifically by EphB3 and EphB2 in a **ligand**-dependent fashion. Our observations add the PDZ domain to the group of conserved protein modules such as Src-homology-2 (SH2) and phosphotyrosine-binding (PTB) domains that regulate signal transduction through their ability to mediate the interaction with RTKs.

L8 ANSWER 59 OF 76 MEDLINE DUPLICATE 26
ACCESSION NUMBER: 1999038246 MEDLINE
DOCUMENT NUMBER: 99038246 PubMed ID: 9819428
TITLE: Delta-1 activation of notch-1 signaling results in HES-1 transactivation.
AUTHOR: Jarriault S; Le Bail O; Hirsinger E; Pourquie O; Logeat F; Strong C F; Brou C; Seidah N G; Isra l A
CORPORATE SOURCE: Unite de Biologie Moleculaire de l'Expression Genique, URA 1773 CNRS, Institut Pasteur, 75724 Paris Cedex 15, France.
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1998 Dec) 18 (12) 7423-31. Journal code: NGY; 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20000330
Entered Medline: 19981224

AB The **Notch** receptor is involved in many cell fate determination events in vertebrates and invertebrates. It has been shown in Drosophila melanogaster that Delta-dependent **Notch** signaling activates the transcription factor Suppressor of Hairless, leading to an increased expression of the Enhancer of Split genes. Genetic evidence has also implicated the kuzbanian gene, which encodes a disintegrin metalloprotease, in the **Notch** signaling pathway. By using a two-cell coculture assay, we show here that vertebrate Dl-1 activates the **Notch**-1 cascade. Consistent with previous data obtained with active forms of **Notch**-1 a HES-1-derived promoter construct is transactivated in cells expressing **Notch**-1 in response to Dl-1 stimulation. Impairing the proteolytic maturation of the full-length receptor leads to a decrease in HES-1 transactivation, further supporting the hypothesis that only mature processed **Notch** is expressed at the cell surface and activated by its **ligand**. Furthermore, we observed that Dl-1-induced HES-1 transactivation was dependent both on Kuzbanian and RBP-J activities, consistent with the involvement of these two proteins in **Notch** signaling in Drosophila. We also observed that exposure of **Notch**-1-expressing cells to Dl-1 results in an increased level of endogenous HES-1 mRNA. Finally, coculture of Dl-1-expressing cells with myogenic C2 cells suppresses differentiation of C2 cells into myotubes, as previously demonstrated for **Jagged**-1 and **Jagged**-2, and also leads to an increased level of endogenous HES-1 mRNA. Thus, Dl-1 behaves as a functional **ligand** for **Notch**-1 and has the same ability to suppress cell differentiation as the **Jagged** proteins do.

L8 ANSWER 60 OF 76 MEDLINE DUPLICATE 27
ACCESSION NUMBER: 1998261432 MEDLINE
DOCUMENT NUMBER: 98261432 PubMed ID: 9596653
TITLE: The **Notch ligand, Jagged**-1, influences the development of primitive hematopoietic precursor cells.
AUTHOR: Varnum-Finney B; Purton L E; Yu M; Brashem-Stein C; Flowers D; Staats S; Moore K A; Le Roux I; Mann R; Gray G; Artavanis-Tsakonas S; Bernstein I D
CORPORATE SOURCE: Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA 98109-1024, USA.
CONTRACT NUMBER: HL54881 (NHLBI)
HL58739-01 (NHLBI)
NS26084 (NINDS)
+
SOURCE: BLOOD, (1998 Jun 1) 91 (11) 4084-91. Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980713
Last Updated on STN: 19980713
Entered Medline: 19980626

AB We examined the expression of two members of the **Notch** family, **Notch**-1 and **Notch**-2, and one **Notch ligand**, **Jagged**-1, in hematopoietic cells. Both **Notch**-1 and **Notch**-2 were detected in murine marrow precursors (Lin-Sca-1+c-kit+). The **Notch ligand**, **Jagged**-1, was not detected in whole marrow or in precursors. However, **Jagged**-1 was seen in cultured primary murine fetal liver stroma, cultured primary murine bone marrow stroma, and in stromal cell lines. These results indicate a potential role for **Notch**-**Notch ligand** interactions in hematopoiesis. To further test this possibility, the effect of **Jagged**-1 on murine marrow precursor cells was assessed by coculturing sorted precursor cells (Lin-Sca-1+c-kit+) with a 3T3 cell layer that expressed human **Jagged**-1 or by incubating sorted precursors with beads coated with the purified extracellular domain of human **Jagged**-1 (**Jagged**-1(ext)). We found that **Jagged**-1, presented both on the cell surface and on beads, promoted a twofold to threefold increase in the formation of primitive precursor cell populations. These results suggest a potential use for **Notch ligands** in expanding precursor cell populations in vitro.

L8 ANSWER 61 OF 76 MEDLINE DUPLICATE 28
ACCESSION NUMBER: 1998384211 MEDLINE
DOCUMENT NUMBER: 98384211 PubMed ID: 9716576
TITLE: Stromal expression of Jagged 1 promotes colony formation by fetal hematopoietic progenitor cells.
AUTHOR: Jones P; May G; Healy L; Brown J; Hoyne G; Delassus S; Enver T
CORPORATE SOURCE: Section of Gene Function and Regulation & Leukaemia Research Fund Centre, Chester Beatty Laboratories, Institute of Cancer Research, London, UK.
SOURCE: BLOOD, (1998 Sep 1) 92 (5) 1505-11.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 20000303
Entered Medline: 19980910

AB The **Notch** signaling system regulates proliferation and differentiation in many tissues. **Notch** is a transmembrane receptor activated by **ligands** expressed on adjacent cells. Hematopoietic stem cells and early progenitors express **Notch**, making the stromal cells which form cell-cell contacts with progenitor cells candidate **ligand**-presenting cells in the hematopoietic microenvironment. Therefore, we examined primary stromal cell cultures for expression of **Notch ligands**. Using reverse transcription-polymerase chain reaction, in situ hybridization, immunohistochemistry, and Western blotting, we demonstrate expression of **Jagged** 1 in primary stromal cultures. To investigate if the stromal expression of **Jagged** 1 has functional effects on hematopoietic progenitors, we cultured CD34(+), c-kit+ hematopoietic progenitor cells derived from the aorto gonadal mesonephros region of day 11 mouse embryos on the **Jagged** 1(-) stromal cell line S17 and on S17 cells engineered to express **Jagged** 1. The presence of **Jagged** 1 increased the number of colonies formed in subsequent methylcellulose culture fourfold. Larger increases in colony numbers were observed under the same culture conditions with CD34(+), c-kit+ hematopoietic progenitor cells derived from d11 fetal liver. These results obtained in vitro table **Jagged** 1 as a candidate regulator of stem cell fate in the context of stromal microenvironments in vivo.

L8 ANSWER 62 OF 76 MEDLINE DUPLICATE 29
ACCESSION NUMBER: 1998367022 MEDLINE
DOCUMENT NUMBER: 98367022 PubMed ID: 9700188
TITLE: Mutational analysis of the Jagged 1 gene in Alagille syndrome families.
AUTHOR: Yuan Z R; Kohsaka T; Ikegaya T; Suzuki T; Okano S; Abe J; Kobayashi N; Yamada M
CORPORATE SOURCE: National Children's Medical Research Center, 3-35-31 Taishido, Setagaya-ku, Tokyo 154, Japan and National Children's Hospital, Tokyo, Japan.
SOURCE: HUMAN MOLECULAR GENETICS, (1998 Sep) 7 (9) 1363-9.
Journal code: BRC; 9208958. ISSN: 0964-6906.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981029
Last Updated on STN: 19981029
Entered Medline: 19981016

AB Alagille syndrome (AGS) is an autosomal dominant disease characterized by five major abnormalities in the liver, heart, face, vertebrae and eye. The responsible gene has been recently identified as the human **Jagged** 1 (JAG1) gene, which encodes a **ligand** for the **Notch** receptor. We analyzed the JAG1 gene in eight AGS families, including affected and unaffected individuals, at the genomic DNA level, mainly by single-strand conformational polymorphism (SSCP) and DNA sequencing analysis. Four categories of mutations were identified: (i) four frameshift mutations in exons 9, 22, 24 and 26 were exhibited respectively in affected individuals of four AGS families, which resulted in moving the translational frame of JAG1; (ii) one nonsense mutation, a 1 bp substitution in exon 5 of the EGF-like repeat domain, was detected in two unrelated AGS families, which altered codon 235 from arginine to stop; (iii) one acceptor splice site mutation of exon 5 was revealed in a sporadic patient; and (iv) a 1.3 Mb deletion, which included the entire JAG1 gene, was found in another patient. Our results further demonstrate that AGS is a dominant disease and suggest that the JAG1 gene exerts a fundamental role in regulating genes involved in development.

L8 ANSWER 63 OF 76 MEDLINE DUPLICATE 30
ACCESSION NUMBER: 1999077701 MEDLINE

DOCUMENT NUMBER: 99077701 PubMed ID: 9858728
TITLE: The Notch signalling pathway in hair growth.
AUTHOR: Powell B C; Passmore E A; Nesci A; Dunn S M
CORPORATE SOURCE: Department of Animal Science, University of Adelaide, Waite Campus, Glen Osmond, 5064, Australia..
bpowell@medicine.adelaide.edu.au
SOURCE: MECHANISMS OF DEVELOPMENT, (1998 Nov) 78 (1-2) 189-92.
Journal code: AXF; 9101218. ISSN: 0925-4773.
PUB. COUNTRY: Ireland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990316
Last Updated on STN: 20000330
Entered Medline: 19990304

AB The **Notch** signalling pathway is an important mediator of cell fate selection whose involvement in epidermal appendage formation is now becoming recognised. Hair follicle development and hair formation involve the co-ordinated differentiation of several different cell types in which **Notch** appears to have a role. We report intricate expression patterns for the **Notch**-1 receptor and three **ligands**, Delta-1, **Jagged**-1 and **Jagged**-2 in the hair follicle. **Notch**-1 is expressed in ectodermal-derived cells of the follicle, in the inner cells of the embryonic placode and the follicle bulb, and in the suprabasal cells of the mature outer root sheath. Delta-1 is only expressed during embryonic follicle development and is exclusive to the mesenchymal cells of the pre-papilla located beneath the follicle placode. Expression of **Jagged**-1 or **Jagged**-2 overlaps **Notch**-1 expression at all stages. In mature follicles, **Jagged**-1 and **Jagged**-2 are expressed in complementary patterns in the follicle bulb and outer root sheath, **Jagged**-1 in suprabasal cells and **Jagged**-2 predominantly in basal cells. In the follicle bulb, **Jagged**-2 is localised to the inner (basal) bulb cells next to the dermal papilla which do not express **Notch** -1, whereas **Jagged**-1 expression in the upper follicle bulb overlaps **Notch**-1 expression and correlates with bulb cell differentiation into hair shaft cortical and cuticle keratinocytes.

L8 ANSWER 64 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:530625 BIOSIS
DOCUMENT NUMBER: PREV199799829828
TITLE: Notch receptor activation inhibits oligodendrocyte differentiation.
AUTHOR(S): Wang, S. (1); Disibio, G.; Bush, G.; Weinmaster, G.; Barres, B. A. (1)
CORPORATE SOURCE: (1) Dep. Neurobiol., Stanford Univ. Sch. Med., Stanford, CA 94305-5401 USA
SOURCE: Society for Neuroscience Abstracts, (1997) Vol. 23, No. 1-2, pp. 1689.
Meeting Info.: 27th Annual Meeting of the Society for Neuroscience New Orleans, Louisiana, USA October 25-30, 1997
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; Abstract; Conference
LANGUAGE: English

L8 ANSWER 65 OF 76 MEDLINE DUPLICATE 31
ACCESSION NUMBER: 97160650 MEDLINE
DOCUMENT NUMBER: 97160650 PubMed ID: 9006984
TITLE: The expression and function of Notch pathway genes in the developing rat eye.
AUTHOR: Bao Z Z; Cepko C L
CORPORATE SOURCE: Harvard Medical School, Department of Genetics and Howard Hughes Medical Institute, Boston, Massachusetts 02115, USA.
CONTRACT NUMBER: EY 06726-01 (NEI)
EYO 9676 (NEI)
SOURCE: JOURNAL OF NEUROSCIENCE, (1997 Feb 15) 17 (4) 1425-34.
Journal code: JDF; 8102140. ISSN: 0270-6474.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970321
Last Updated on STN: 19970321
Entered Medline: 19970310

AB The **Notch** gene plays a role in the development of disparate tissues in multiple organisms. Because the vertebrate eye is an excellent model system for both patterning and cell fate determination, two processes that can involve **Notch**, we examined the expression patterns of **Notch** 1 and **Notch** 2, and their **ligands** Delta and **Jagged**, in the developing rat eye. **Notch** 1 and Delta were found to be expressed in the neural retina during the period of cell fate determination and differentiation. **Notch** 2 was found to be expressed in the non-neuronal derivatives of the optic cup, including the pigment epithelium, optic stalk, and ciliary body. **Jagged** was expressed in distinct regions within the optic vesicle, ciliary body, and lens, with patterns that changed over time. The potential function of **Notch** 1 in cell-type specification and differentiation was examined by introducing a constitutively active form of **Notch** 1 in vivo using a replication-incompetent retrovirus. This form of **Notch** 1 was found to cause abnormal growth and interfere with the differentiation of multiple retinal cell types.

L8 ANSWER 66 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:68851 BIOSIS
DOCUMENT NUMBER: PREV199800068851
TITLE: Activation of Notch1 by its ligand, Jagged1, inhibits granulocytic differentiation and permits expansion of immature myeloid progenitors.
AUTHOR(S): Milner, L. A.; Li, L.; Hood, L.; Torok-Storb, B.
CORPORATE SOURCE: Fred Hutchinson Cancer Res. Cent., Univ. Washington, Seattle, WA USA
SOURCE: Blood, (Nov. 15, 1997) Vol. 90, No. 10 SUPPL. 1 PART 1, pp. 571A.
Meeting Info.: 39th Annual Meeting of the American Society of Hematology San Diego, California, USA December 5-9, 1997
The American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference

LANGUAGE: English

L8 ANSWER 67 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:68478 BIOSIS
DOCUMENT NUMBER: PREV199800068478
TITLE: Expression of the **notch ligand** **jagged** 1 in bone marrow stromal cells suggests heterotypic interaction may activate **notch** signalling in hematopoietic progenitors.
AUTHOR(S): Jones, P. H.; Healy, L.; Enver, T.
CORPORATE SOURCE: Leukaemia Res. Fund, Chester Beatty Lab., London UK
SOURCE: Blood, (Nov. 15, 1997) Vol. 90, No. 10 SUPPL. 1 PART 1, pp. 488A.
Meeting Info.: 39th Annual Meeting of the American Society of Hematology San Diego, California, USA December 5-9, 1997 The American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 68 OF 76 MEDLINE DUPLICATE 32
ACCESSION NUMBER: 97422615 MEDLINE
DOCUMENT NUMBER: 97422615 PubMed ID: 9268641
TITLE: Identification and cloning of the human homolog (JAG1) of the rat Jagged1 gene from the Alagille syndrome critical region at 20p12.
AUTHOR: Oda T; Elkahloun A G; Meltzer P S; Chandrasekharappa S C
CORPORATE SOURCE: Laboratory of Gene Transfer, National Human Genome Research Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
SOURCE: GENOMICS, (1997 Aug 1) 43 (3) 376-9.
Journal code: GEN; 8800135. ISSN: 0888-7543.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF003837
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 20000303
Entered Medline: 19971103
AB **Notch** proteins are a family of closely related transmembrane receptors proven to be instrumental in cell fate decisions. Recently, **Notch ligands** Delta and **Jagged** have been identified in Drosophila and rat, respectively. We have isolated the human homolog of the rat Jagged1 gene, JAG1, from a CpG island in a YAC clone covering the Alagille syndrome critical region at chromosome 20p12 (tel-SNAP-D20S186-cen). Alagille syndrome is an autosomal dominant disorder characterized by neonatal jaundice, paucity of intrahepatic bile ducts, and abnormalities of the heart, skeleton, and eyes. The human Jagged1 (JAG1), therefore, appears to be a strong candidate gene for this disease. Here we describe the identification, full-length cDNA cloning, expression patterns, and precise physical location of this gene within the Alagille syndrome critical region.

L8 ANSWER 69 OF 76 MEDLINE DUPLICATE 33
ACCESSION NUMBER: 97351505 MEDLINE
DOCUMENT NUMBER: 97351505 PubMed ID: 9207787
TITLE: Mutations in the human Jagged1 gene are responsible for Alagille syndrome.
COMMENT: Comment in: Nat Genet. 1997 Jul;16(3):212-3
AUTHOR: Oda T; Elkahloun A G; Pike B L; Okajima K; Krantz I D; Genin A; Piccoli D A; Meltzer P S; Spinner N B; Collins F S; Chandrasekharappa S C
CORPORATE SOURCE: Laboratory of Gene Transfer, National Human Genome Research Institutes of Health, Bethesda, Maryland 20892-4442, USA.
SOURCE: NATURE GENETICS, (1997 Jul) 16 (3) 235-42.
Journal code: BRO; 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970812
Last Updated on STN: 19970812
Entered Medline: 19970729
AB Alagille syndrome (AGS) is an autosomal-dominant disorder characterized by intrahepatic cholestasis and abnormalities of heart, eye and vertebrae, as well as a characteristic facial appearance. Identification of rare AGS patients with cytogenetic deletions has allowed mapping of the gene of 20p12. We have generated a cloned contig of the critical region and used fluorescent in situ hybridization on cells from patients with submicroscopic deletions to narrow the candidate region to only 250 kb. Within this region we identified JAG1, the human homologue of rat Jagged1, which encodes a **ligand** for the **Notch** receptor.
Cell-cell **Jagged/Notch** interactions are known to be critical for determination of cell fates in early development, making this an attractive candidate gene for a developmental disorder in humans. Determining the complete exon-intron structure of JAG1 allowed detailed mutational analysis of DNA samples from non-deletion AGS patients, revealing three frame-shift mutations, two splice donor mutations and one mutation abolishing RNA expression from the altered allele. We conclude that AGS is caused by haploinsufficiency of JAG1.

L8 ANSWER 70 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:67058 BIOSIS
DOCUMENT NUMBER: PREV199800067058
TITLE: Human notch ligands affect both hematopoietic progenitor and long term-culture initiating cells (LTC-IC) in in vitro culture.
AUTHOR(S): Sakano, S.; Taijma, S.; Miyabayashi, T.; Enomoto, M.; Ninomiya, N.; Nitadori, Y.; Ito, H.; Itoh, A.; Ohno, M.
CORPORATE SOURCE: Life Sci. Fundamental Res. Lab., Asahi Chem. Industry Co. Ltd., Fuji, Shizuoka Japan
SOURCE: Blood, (Nov. 15, 1997) Vol. 90, No. 10 SUPPL. 1 PART 1, pp. 170A.
Meeting Info.: 39th Annual Meeting of the American Society of Hematology San Diego, California, USA December 5-9, 1997 The American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 71 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:67023 BIOSIS
DOCUMENT NUMBER: PREV199800067023
TITLE: The **notch ligand**, **jagged**-1, promotes the formation of increased numbers of a primitive hematopoietic precursor cell.
AUTHOR(S): Varnum-Finney, B.; Purton, L.; Gray, G.; Mann, R.; Artvanis-Tsakonas, S.; Bernstein, I.
CORPORATE SOURCE: Dep. Pediatrics Oncology, Fred Hutchinson Cancer Res. Cent., Seattle, WA USA
SOURCE: Blood, (Nov. 15, 1997) Vol. 90, No. 10 SUPPL. 1 PART 1, pp. 162A.-163A.
Meeting Info.: 39th Annual Meeting of the American Society of Hematology San Diego, California, USA December 5-9, 1997 The American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 72 OF 76 MEDLINE DUPLICATE 34
ACCESSION NUMBER: 97115768 MEDLINE
DOCUMENT NUMBER: 97115768 PubMed ID: 8955070
TITLE: An antisense oligonucleotide to the **notch ligand jagged** enhances fibroblast growth factor-induced angiogenesis in vitro.
AUTHOR: Zimrin A B; Pepper M S; McMahon G A; Nguyen F; Montesano R; Maciag T
CORPORATE SOURCE: Department of Molecular Biology, Holland Laboratory, American Red Cross, Rockville, Maryland 20855, USA.
CONTRACT NUMBER: AG07450 (NIA)
HL02646 (NHLBI)
HL32348 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Dec 20) 271 (51) 32499-502.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U77720; GENBANK-U77914
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19980206
Entered Medline: 19970123
AB Angiogenesis, or the formation of new blood vessels, plays a central role in a number of physiologic and pathologic conditions, including wound healing, diabetic retinopathy, and solid tumor growth, and endothelial cells can be induced to mimic this process in vitro. Using a modification of the differential display method (Zimrin, A. B., Villeponteau, B., and Maciag, T. (1995) Biochem. Biophys. Res. Commun. 213, 630-638), we isolated the human homolog of the **Jagged ligand** for the **Notch** receptor from human endothelial cells exposed to fibrin and demonstrate that the **Jagged** transcript, but not the **Notch** 1 or **Notch** 2 transcripts, are up-regulated by fibrin. Interestingly, the addition of an antisense **Jagged** oligomer to bovine microvascular endothelial cells grown on a collagen gel resulted in a marked increase in invasion and tube formation in the underlying gel in response to fibroblast growth factor. In contrast, no effect was observed on vascular endothelial growth factor-induced angiogenesis under identical conditions. These data suggest that **Jagged**-**Notch** signaling is able to regulate fibroblast growth factor-induced endothelial cell migration in vitro, an early event during angiogenesis in vivo.

L8 ANSWER 73 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:308011 BIOSIS
DOCUMENT NUMBER: PREV199699030367
TITLE: An antisense oligonucleotide to the **notch ligand jagged** promotes angiogenesis in bovine microvascular endothelial cells (BMEC) on collagen gels.
AUTHOR(S): Zimrin, A. B. (1); Pepper, M. S.; Montesano, R.; Maciag, T.
CORPORATE SOURCE: (1) Holland Lab., Rockville, MD 20855 USA
SOURCE: FASEB Journal, (1996) Vol. 10, No. 6, pp. A1094.
Meeting Info.: Joint Meeting of the American Society for Biochemistry and Molecular Biology, the American Society for Investigative Pathology and the American Association of Immunologists New Orleans, Louisiana, USA June 2-6, 1996
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 74 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:201006 BIOSIS
DOCUMENT NUMBER: PREV199698757135
TITLE: Expression of the putative **notch**-1 **ligands**, delta-1 and **jagged** in the developing vertebrate retina.
AUTHOR(S): Ahmad, Iqbal; Polk, Dorisa; Dooley, Constance
CORPORATE SOURCE: Dep. Cell Biology Anatomy, Univ. Nebr. Med. Cent., Omaha, NE USA
SOURCE: Investigative Ophthalmology & Visual Science, (1996) Vol. 37, No. 3, pp. S200.
Meeting Info.: 1996 Annual Meeting of the Association for Research in Vision and Ophthalmology Fort Lauderdale, Florida, USA April 21-26, 1996
ISSN: 0146-0404.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 75 OF 76 MEDLINE DUPLICATE 35
ACCESSION NUMBER: 97082209 MEDLINE
DOCUMENT NUMBER: 97082209 PubMed ID: 8923452
TITLE: Expression patterns of Jagged, Delta1, Notch1, Notch2, and Notch3 genes identify ligand-receptor pairs that may function in neural development.
AUTHOR: Lindsell C E; Boulter J; diSibio G; Gossler A; Weinmaster G
CORPORATE SOURCE: Department of Biological Chemistry, UCLA School of Medicine 90095-1737, USA.
CONTRACT NUMBER: GM08042 (NIGMS)
NS1885-01 (NINDS)
SOURCE: MOLECULAR AND CELLULAR NEUROSCIENCES, (1996) 8 (1) 14-27.
Journal code: B1D; 9100095. ISSN: 1044-7431.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970305
Last Updated on STN: 19970305
Entered Medline: 19970220

AB **Notch** genes encode receptors for a signaling pathway that regulates neurogenesis. The DSL (Delta/Serrate/lag-2) genes encode **ligands** that bind and activate **Notch**. In situ hybridization was used to determine the spatiotemporal expression of Notch1, Notch2, and Notch3, and the DSL **ligands**, **Jagged** and Delta 1, in an effort to identify potential **ligand**-receptor pairs that function during development of the rat nervous system. Here we describe both distinct and overlapping expression patterns for these genes in neural progenitors that form both the central and the peripheral nervous systems. The punctate expression patterns we detected for **Jagged** and Delta 1 are consistent with their role in mediating lateral inhibition, a process proposed to regulate neural determination. Furthermore, within the ventricular zone of the neural tube and retina, **Jagged** and Delta 1 were expressed in complementary regions, suggesting that different DSL-**Notch** combinations may direct the development of distinct neural subtypes.

L8 ANSWER 76 OF 76 MEDLINE DUPLICATE 36
ACCESSION NUMBER: 95211842 MEDLINE
DOCUMENT NUMBER: 95211842 PubMed ID: 7697721
TITLE: Jagged: a mammalian ligand that activates Notch1.
AUTHOR: Lindsell C E; Shawber C J; Boulter J; Weinmaster G
CORPORATE SOURCE: Department of Biological Chemistry School of Medicine, University of California, Los Angeles 90024.
CONTRACT NUMBER: NS31885-01 (NINDS)
SOURCE: CELL, (1995 Mar 24) 80 (6) 909-17.
Journal code: CQ4; 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-L38483; GENBANK-U61276
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950510
Last Updated on STN: 19980206
Entered Medline: 19950501

AB Here we report the isolation of a rat cDNA clone, **Jagged**, which we show encodes a **ligand** for vertebrate **Notch**. Our conclusion is based on three observations. First, sequence analysis reveals substantial homology between **Jagged** and invertebrate **ligands** for the LIN-12/**Notch** proteins. Second, in situ hybridization of rat embryos identifies both distinct and overlapping patterns of gene expression for **Jagged** with those for Notch1, Notch2, and Notch3. Finally, the biological activity of **Jagged** was tested using a cell culture assay in which **Jagged** activates rat Notch1 expressed in myoblasts and prevents muscle cell differentiation. Our data support the hypothesis that **Notch**-**ligand** interactions function in maintaining mammalian cells in an undifferentiated state.

=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:n

=> dis his

(FILE 'HOME' ENTERED AT 11:18:57 ON 24 FEB 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 11:19:07 ON 24 FEB 2002
L1 240 S JAGGED (P) NOTCH
L2 0 S (ADMINIST? (10N) JAGGED) (P) NOTCH
L3 0 S (ADMINIST? (10N) JAGGED)
L4 12 S (ADMINIST? (P) JAGGED)
L5 6 DUP REM L4 (6 DUPLICATES REMOVED)
L6 180 S L1 (P) LIGAND
L7 0 S L6 (P) (PHARMACEUT? OR THERAP?)
L8 76 DUP REM L6 (104 DUPLICATES REMOVED)

=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	137.51	137.66

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.72	-3.72

STN INTERNATIONAL LOGOFF AT 11:38:47 ON 24 FEB 2002

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=> dis his

     (FILE 'HOME' ENTERED AT 17:46:43 ON 23 FEB 2002)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 17:46:59 ON 23 FEB 2002
L1          1390 S LAMBJ?/AU OR DALLMAN M?/AU OR HOYNE G?/AU
L2          4132 S LAMB J?/AU OR DALLMAN M?/AU OR HOYNE G?/AU
L3            28 S L2 AND NOTCH
L4            13 DUP REM L3 (15 DUPLICATES REMOVED)
L5             1 S ADMIST? (P) (NOTCH OR SERRATE OR SER OR DELTA)
L6         22582 S ADMINIST? (P) (NOTCH OR SERRATE OR SER OR DELTA)
L7         22425 S ADMINIST? (P) (SERRATE OR SER OR DELTA)
L8             4 S ( ADMINIST? (P) (SERRATE OR SER OR DELTA)) AND NOTCH
L9             3 DUP REM L8 (1 DUPLICATE REMOVED)

=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    75.45      75.60

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -3.10      -3.10

STN INTERNATIONAL LOGOFF AT 17:54:29 ON 23 FEB 2002
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=> s LambJ?/au or Dallman M?/au or Hoyne G?/au
L1        1390 LAMBJ?/AU OR DALLMAN M?/AU OR HOYNE G?/AU

=> s Lamb J?/au or Dallman M?/au or Hoyne G?/au
L2        4132 LAMB J?/AU OR DALLMAN M?/AU OR HOYNE G?/AU

=> s l2 and notch
L3          28 L2 AND NOTCH

=> dup rem l28
L28 IS NOT VALID HERE
The L-number entered has not been defined in this session, or it
has been deleted.  To see the L-numbers currently defined in this
session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4          13 DUP REM L3 (15 DUPLICATES REMOVED)

=> dis l4 1-13 ibib abs

L4   ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        2002:123354  CAPLUS
TITLE:                   Assay
INVENTOR(S):             Lamb, Jonathan Robert; Hoyne, Gerard
                         Francis; Dallman, Margaret Jane;
                         Champion, Brian Robert
PATENT ASSIGNEE(S):      Lorantis Limited, UK
SOURCE:                  PCT Int. Appl., 75 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2002012890      A2   20020214       WO 2001-GB3503   20010803
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
             UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                  GB 2000-19242    A  20000804
AB   A method for monitoring the immune system comprising monitoring the
     Notch signalling pathway.

L4   ANSWER 2 OF 13  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        2001:380426  CAPLUS
DOCUMENT NUMBER:         135:9978
TITLE:                   Immunotherapy with genetically engineered
                         tumor-infiltrating lymphocytes
INVENTOR(S):             Lamb, Jonathan Robert; Hoyne, Gerard
                         Francis
PATENT ASSIGNEE(S):      Lorantis Ltd., UK
SOURCE:                  PCT Int. Appl., 34 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2001035990      A2   20010525       WO 2000-GB4391   20001117
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                  GB 1999-27328    A  19991118
AB   A method is provided for enhancing the reactivity of a T cell toward a
     tumor cell which method comprises: (a) isolating a T cell which is a
     tumor-infiltrating lymphocyte (TIL) from a patient having said tumor cell
     present in their body; (b) introducing a nucleic acid sequence into the
     TIL, which sequence is capable of inhibiting or preventing expression of
     an endogenous Notch ligand in the TIL; and (c) re-introducing
     the transfected TIL into the patient; wherein the T cell comprises a T
     cell receptor specific for a tumor antigen expressed by the tumor cell.

L4   ANSWER 3 OF 13     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:   2001677038     MEDLINE
DOCUMENT NUMBER:    21579863   PubMed ID: 11722637
TITLE:              Notch signalling in the regulation of peripheral
                    immunity.
AUTHOR:             Hoyne G F; Dallman M J; Champion B R;
                    Lamb J R
CORPORATE SOURCE:   Immunobiology Group, Department of Pathology, Respiratory
                    Medicine Unit, MRC Centre of Inflammation Research,
                    University of Edinburgh, Edinburgh, UK.. g.hoyne@ed.ac.uk
SOURCE:             IMMUNOLOGICAL REVIEWS, (2001 Aug) 182 215-27.  Ref: 81
                    Journal code: 7702118. ISSN: 0105-2896.
PUB. COUNTRY:       Denmark
                    Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
                    (REVIEW, TUTORIAL)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200202
ENTRY DATE:         Entered STN: 20011128
                    Last Updated on STN: 20020209
                    Entered Medline: 20020208
AB   Notch signalling plays a critical role in embryogenesis,
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influencing the differentiation and growth of a variety of cell types across the species. In the mammalian immune system, **Notch** signalling operates at various levels; it controls the differentiation of haematopoietic stem cells and directs the early development of the T and B-cell lineages. It is also involved in the maturation of both CD4+ and CD8+ T cells in the thymus. The biological activities of this pathway extend beyond lymphocyte ontogeny; recent evidence has shown that it also contributes to the regulation of the peripheral immune system through its ability to influence cell survival and growth. In fulfilling this function, **Notch** signalling appears to act in conjunction with defined immunological signals such as cytokines, T-cell antigen receptor and co-stimulatory receptor-mediated signalling. In this review we discuss the potential of the **Notch** signalling pathway in the maintenance of homeostasis within the immune system affecting both peripheral tolerance and the negative feedback controlling productive immunity. The therapeutic manipulation of this pathway is likely to have broad application in a range of immunologically based diseases.

L4 ANSWER 4 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:178247 BIOSIS
DOCUMENT NUMBER: PREV200100178247
TITLE: Regulatory T cells: A role for **notch** signalling.
AUTHOR(S): **Lamb, J. (1); Dallman, M. J. (1); Hoyne, G. F. (1)**
CORPORATE SOURCE: (1) University of Edinburgh and Imperial College of Science, Technology and Medicine, London UK
SOURCE: Clinical and Experimental Allergy, (January, 2001) Vol. 31, No. 1, pp. 165. print.
Meeting Info.: Annual Meeting of the British Society for Allergy and Clinical Immunology Nottingham, England August 02-03, 2000 British Society for Allergy and Clinical Immunology
. ISSN: 0954-7894.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L4 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:421290 CAPLUS
DOCUMENT NUMBER: 133:72935
TITLE: Methods of immunosuppression
INVENTOR(S): **Lamb, Jonathan Robert; Dallman, Margaret Jane; Hoyne, Gerard Francis**
PATENT ASSIGNEE(S): Lorantis Ltd., UK
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000036089	A2	20000622	WO 1999-GB4233	19991215
WO 2000036089	A3	20001026		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1141243	A2	20011010	EP 1999-961206	19991215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001048930	A1	20011206	US 2001-870902	20010531

PRIORITY APPLN. INFO.: GB 1998-27604 A 19981215
WO 1999-GB4233 W 19991215

AB A method for producing a T cell having tolerance to an allergen or antigen which method comprises incubating the T cell with an antigen presenting cell (APC) in the presence of (i) a compn. capable of upregulating expression of an endogenous **Notch** ligand in the APC and (ii) the allergen or antigen is provided. The **Notch** or **Notch** ligand-upregulating compn. comprises a polypeptide selected from Noggin, Chordin, Follistatin, Xnr3, FGF or deriv.; and an immunosuppressive cytokine selected from IL-4, IL-10, IL-13, TGF-.beta. and FLT3.

L4 ANSWER 6 OF 13 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000404250 MEDLINE
DOCUMENT NUMBER: 20387636 PubMed ID: 10929049
TITLE: T-cell regulation of peripheral tolerance and immunity: the potential role for **Notch** signalling.
AUTHOR: **Hoyne G F; Dallman M J; Lamb J R**
CORPORATE SOURCE: Immunobiology Group, MRC Centre for Inflammation Research and the Respiratory Medicine Unit, University of Edinburgh, Teviot Place, Edinburgh, UK.
SOURCE: IMMUNOLOGY, (2000 Jul) 100 (3) 281-8. Ref: 36
Journal code: GH7; 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000901
Last Updated on STN: 20000901
Entered Medline: 20000821

AB Recognition of antigen by T cells in the periphery may lead either to the generation of productive immunity or the induction of tolerance. These two functional outcomes are a consequence of distinct pathways of T-cell differentiation. T cells are selected to become regulatory cells and their function is to maintain homeostasis with the immune system. In this review we discuss the cell-fate decisions that T cells might make allowing them to promote immunity or induce tolerance in the context of the role that **Notch** signalling may play in this process.

L4 ANSWER 7 OF 13 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2000120669 MEDLINE

DOCUMENT NUMBER: 20120669 PubMed ID: 10653853
TITLE: Serrate1-induced **notch** signalling regulates the decision between immunity and tolerance made by peripheral CD4(+) T cells.
AUTHOR: **Hoyne G F**; Le Roux I; Corsin-Jimenez M; Tan K; Dunne J; Forsyth L M; **Dallman M J**; Owen M J; Ish-Horowicz D; **Lamb J R**
CORPORATE SOURCE: Respiratory Medicine Unit, University of Edinburgh Medical School, Teviot Place, Edinburgh EH8 9AG, UK.
SOURCE: INTERNATIONAL IMMUNOLOGY, (2000 Feb) 12 (2) 177-85. Journal code: AY5; 8916182. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000505
Last Updated on STN: 20000505
Entered Medline: 20000424

AB Signals derived from antigen-presenting cells (APC) influence the functional differentiation of CD4(+) T cells. We report here that Serrate1 (Jagged1), a ligand for the Notch1 receptor, may contribute to the differentiation of peripheral CD4(+) T cells into either helper or regulatory cells. Our findings demonstrate that antigen presented by murine APC overexpressing human Serrate1 induces naive peripheral CD4(+) T cells to become regulatory cells. These cells can inhibit primary and secondary immune responses, and transfer antigen-specific tolerance to recipient mice. Our results show that **Notch** signalling may help explain 'linked' suppression in peripheral tolerance, whereby tolerance induced to one epitope encompasses all epitopes on that antigen during the course of an immune response.

L4 ANSWER 8 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:82870 BIOSIS
DOCUMENT NUMBER: PREV200100082870
TITLE: Use of conditional transgenic mice to study the role of **Notch** signaling in T cells.
AUTHOR(S): Tan, Karen (1); **Lamb, Jonathan R. (1)**; **Hoyne, Gerard F. (1)**
CORPORATE SOURCE: (1) Immunobiology Group, MRC Centre for Inflammation Research, University of Edinburgh Medical School, Teviot Place, Edinburgh, EH8 9AG UK
SOURCE: Immunology, (December, 2000) Vol. 101, No. Supplement 1, pp. 20. print.
Meeting Info.: Annual Congress of the British Society for Immunology Harrogate, UK December 05-08, 2000 British Society for Immunology
. ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L4 ANSWER 9 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:82827 BIOSIS
DOCUMENT NUMBER: PREV200100082827
TITLE: Role of the jagged/**notch** gene family in T-cell activation versus anergy.
AUTHOR(S): Ponchel, Frederique (1); Ali, Manir (1); Verhoef, Adrienne (1); **Lamb, Jonathan (1)**; Isaacs, John (1)
CORPORATE SOURCE: (1) Molecular Medicine Unit, University of Leeds, Leeds UK
SOURCE: Immunology, (December, 2000) Vol. 101, No. Supplement 1, pp. 8. print.
Meeting Info.: Annual Congress of the British Society for Immunology Harrogate, UK December 05-08, 2000 British Society for Immunology
. ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L4 ANSWER 10 OF 13 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1999242412 MEDLINE
DOCUMENT NUMBER: 99242412 PubMed ID: 10224357
TITLE: Linked suppression in peripheral T cell tolerance to the house dust mite derived allergen Der p 1.
AUTHOR: **Hoyne G F**; **Dallman M J**; **Lamb J R**
CORPORATE SOURCE: Respiratory Medicine Unit, Edinburgh University Medical School, Edinburgh, UK.
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1999 Feb-Apr) 118 (2-4) 122-4.
Journal code: BJ7; 9211652. ISSN: 1018-2438.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990618
Last Updated on STN: 19990618
Entered Medline: 19990610

AB BACKGROUND: Peripheral tolerance is required to maintain balance within the immune system. A feature of peripheral tolerance is linked suppression, in which tolerance induced to a single T cell epitope inhibits the response to all epitopes in the same protein. It is suggested that this phenomenon is mediated by regulatory T cells through either the activity of immunopressive cytokines or direct cell contact. In previous experiments we failed to detect inhibitory cytokines when T cells from mice rendered tolerant by intranasal delivery of the immunodominant peptide of Der p 1 (p 1, 110-131) were restimulated with peptide in vitro. Therefore, the aim of this study was to determine if cognate interactions between T cells mediated by **Notch**/Delta signaling induce and maintain peripheral T cell tolerance. METHODS: Using in situ hybridization and viral mediated gene transfer, the expression and function of Delta1 were investigated in a murine model of T cell tolerance to Der p 1 in vivo. RESULTS: Delta1 expression is increased on peripheral T cells during the induction of tolerance with high-dose peptide delivered intranasally and when tolerant animals are rechallenged under immunogenic conditions. Peptide p 1, 110-131-specific CD4+ T cells transfected with Delta1 inhibited the response of antigen-primed T cells and induced linked suppression. CONCLUSIONS: High-dose peptide delivered intranasally induces transient expression of Delta 1 on inhibitory CD4+ T cells. Ligation of the Notch1 receptor on neighbouring T cells by Delta1+ regulatory T cells

inhibits clonal expansion of the former and mediates linked suppression.

L4 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:324898 CAPLUS
DOCUMENT NUMBER: 128:320575
TITLE: Controlling abnormal immune responses by modulation of the interactions between members of the **Notch** family of proteins
INVENTOR(S): **Lamb, Jonathan Robert; Dallman, Margaret Jane; Hoyne, Gerald Francis**
PATENT ASSIGNEE(S): Imperial College of Science Technology & Medicine, UK; Lamb, Jonathan Robert; Dallman, Margaret Jane; Hoyne, Gerald Francis
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9820142	A1	19980514	WO 1997-GB3058	19971106
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9748765	A1	19980529	AU 1997-48765	19971106
AU 736361	B2	20010726		
GB 2335194	A1	19990915	GB 1999-10276	19971106
GB 2335194	B2	20010425		
EP 942998	A1	19990922	EP 1997-911353	19971106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1242802	A	20000126	CN 1997-181159	19971106
GB 2353094	A1	20010214	GB 2000-23691	19971106
GB 2353094	B2	20010613		
JP 2001504331	T2	20010403	JP 1998-521150	19971106
NO 9902196	A	19990705	NO 1999-2196	19990505

PRIORITY APPLN. INFO.:
GB 1996-23236 A 19961107
GB 1997-15674 A 19970724
GB 1997-19350 A 19970911
GB 1999-10276 A3 19971106
WO 1997-GB3058 W 19971106

AB Methods of modifying the interaction of components such as T-cells, T-cell-antigen presenting cells (APC) and between pathogenic organisms and immunocompetent cells of a host using members of the **Notch** protein family and their ligands are described. Hybridoma cells expressing the gene for Delta protein were shown to prevent antigen-primed lymphocytes from proliferating upon exposure to the priming antigen. Dendritic cells expressing the Serrate gene prevented the antigen priming of T cells. The use T cell hybridomas expressing the Delta gene to inhibit the development of immunity to the Der p 1 is demonstrated.

L4 ANSWER 12 OF 13 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1998384211 MEDLINE
DOCUMENT NUMBER: 98384211 PubMed ID: 9716576
TITLE: Stromal expression of Jagged 1 promotes colony formation by fetal hematopoietic progenitor cells.
AUTHOR: Jones P; May G; Healy L; Brown J; **Hoyne G**; Delassus S; Enver T
CORPORATE SOURCE: Section of Gene Function and Regulation & Leukaemia Research Fund Centre, Chester Beatty Laboratories, Institute of Cancer Research, London, UK.
SOURCE: BLOOD, (1998 Sep 1) 92 (5) 1505-11.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 20000303
Entered Medline: 19980910

AB The **Notch** signaling system regulates proliferation and differentiation in many tissues. **Notch** is a transmembrane receptor activated by ligands expressed on adjacent cells. Hematopoietic stem cells and early progenitors express **Notch**, making the stromal cells which form cell-cell contacts with progenitor cells candidate ligand-presenting cells in the hematopoietic microenvironment. Therefore, we examined primary stromal cell cultures for expression of **Notch** ligands. Using reverse transcription-polymerase chain reaction, in situ hybridization, immunohistochemistry, and Western blotting, we demonstrate expression of Jagged 1 in primary stromal cultures. To investigate if the stromal expression of Jagged 1 has functional effects on hematopoietic progenitors, we cultured CD34(+), c-kit+ hematopoietic progenitor cells derived from the aorto gonadal mesonephros region of day 11 mouse embryos on the Jagged 1(-) stromal cell line S17 and on S17 cells engineered to express Jagged 1. The presence of Jagged 1 increased the number of colonies formed in subsequent methylcellulose culture fourfold. Larger increases in colony numbers were observed under the same culture conditions with CD34(+), c-kit+ hematopoietic progenitor cells derived from d11 fetal liver. These results obtained in vitro table Jagged 1 as a candidate regulator of stem cell fate in the context of stromal microenvironments in vivo.

L4 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1947:9010 CAPLUS